THE

Journal of Obstetrics & Gynaecology of the British Empire

VOL. 54, No. 4 NEW SERIES AUGUST 1947

Sedation with Rectal Tri-brom-ethanol (Avertin, Bromethol) in the Management of Eclampsia

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INTRODUCTION

THE aetiology of eclampsia still evades detection, and the basis of treatment, therefore, remains unsatisfactory. The complete absence of any specific therapy compels the adoption of treatment based either on the relief of the individual clinical manifestations of the disease or upon the various and unproved theories of the cause.

Of these procedures the greatest reputation belongs to the sedative management associated with the name of Stroganoff; to the eliminative method at one time so popular in Dublin, and to combinations of these two procedures. It is true that sedation and elimination cannot be regarded as completely compatible one with another, but the attempt to combine them was at one time commonly practised. [The authors of this paper, however, have completely abandoned the so-called eliminative management.] The results of a purely surgical approach to the disease have not been impressive. The condemnation of methods of *accouchement forcé* in the management of eclampsia—as in other spheres—is now universal, and Caesarean section has a somewhat sinister reputation.

The choice of sedative in eclampsia is comparatively restricted. The quick effect of chloroform has led to its occasional use, despite its well-known dangers, but for more prolonged sedation the choice has fallen in general upon morphia, certain barbiturates, chloral and paraldehyde. The authors' experience with these drugs has not been wholly satisfactory, since it has not been possible with any certainty to prevent recurrence of seizures, and since dangerous respiratory depression of mother and child has been common when the drugs were pushed. One of us (J. B. D.), impressed by the admirable pre-anaesthetic sedation obtained by the use of tri-brom-ethanol, conceived the idea of using it in eclampsia. Originality cannot be claimed for this use of the drug by either of the authors, but both have been using it since

1943 in two hospitals which together admit virtually all obstetrical emergencies occurring in the counties of Ayr, Dumfries, Kirkcudbright and Wigtown (population approximately 500,000), and they believe that their results have been sufficiently favourable to justify this presentation.

Literature

Tri-brom-ethanol, first introduced as a basal anaesthetic, was later employed as an obstetrical analgesic. Its physical, chemical, and pharmacological properties have been repeatedly described and it is not proposed to recapitulate them.

The use of the drug as an anticonvulsant in tetanus appears to have been suggested early (Läwen, 1927, 1928; Huntingdon, 1931; Sartorius, 1933; Boyce and McFetridge, 1935; Mitchell, 1935; Cole, 1935; Freeman, 1936), and the literature includes statements of its use in eclampsia, of which we have been able to trace those by Conrad (1927), Benhline (1927), Sennewald (1928), Shipley and Cairns (1930), Pierce (1931), Coghlan (1931), Morrison (1931), Whitaker (1933), Carré and Gellé (1938), Gellé (1939), and Miller (1944). There does not appear to have been any publication which included any series of cases sufficiently large to warrant the drawing of statistically significant conclusions, most of the references quoted being descriptions of comparatively few cases with favourable results, without any attempts to produce comprehensive surveys of all cases treated in the clinics concerned.

Cases Presented in the Present Survey

The patients were drawn from the counties already enumerated. With few exceptions the Ayrshire cases came from an industrial population, the remainder from a mainly agricultural area.

Since January 1st, 1943, all cases under the authors' care were treated by tri-brom-ethanol, except for 4 cases (including 1 fatality) short details of which appear in Table I.

Table I

Eclamptic patients since introduction of Bromethol treated otherwise and omitted from series.

Case A	Admitted on second day of puerperium with multiple mid-brain plegias following intrapartum eclampsia treated by family doctor. Did not require sedation. Mother and child survived.
Case B	Single and immediately fatal seizure followed 12 hours after mid-forceps delivery of patient, who had been under observation for moderate hypertension for 1 month prior to delivery. Death occurred too quickly for any treatment to be instituted. Child survived.
Case C	After 2 eclamptic seizures at home, developed concealed accidental haemorrhage. Judged too collapsed to justify or to require energetic sedation. Treated by artificial rupture of membranes and transfusion, had 1 eclamptic seizure following recovery from shock, but survived. Baby stillborn.
Case D	Admitted at term in labour, with severe pre-eclampsia, with head on perineum. Developed one eclamptic convulsion. Delivered immediately by low forceps under general anaesthesia. Further seizures judged unlikely, no sedation given. Both survived.

A total of 44 cases is described. Of these 29 cases were treated in Ayrshire, 15 in Dumfries. Although journeys by ambulance were often long and rough, no attempt was made to avoid them, and all cases were eventually admitted to hospital.

Full details of individual cases will be found in Table II.

Case number	Date of admission	Age	Parity	Maturity on delivery (weeks)	Blood-pressure (mm. Hg.)	Urine			Fits	
						Albumen g. per litre	Output in 1st 24 hours (ml.)	Oedema	Before bromethol	After brometho
1.	1942	23	0	34	120/80	+++	1920	+	7	0
2.	1943	31	1	35	150/100	+	1440	Nil	3	0
3.	1943	23	0	37	100/65	16	480	Nil	4	0
4.	1943	24	0	39	170/95	12	2280	++	1	0
5.	1943	32	0	40	145/105	+++	480	++	2	0
6.	1943	28	0	35	180/120	2	360	+	1	0
7.	1943	30	0	36	218/130	14	240	+++	2	0
8.	1943	25	2	40	190/120	6	300	+	3	0
9.	1944	25	1	37	170/120	13	180	+++	4	0
10.	1944	20	0	39	190/110	8	480	+	3	0
11.	1944	35	4	40	125/85	Nil	?	Nil	1	0
12.	1944	20	0	39	190/125	16	1140	+++	2	0
13.	1944	23	2	38	179/100	8	?	+	5	5
14.	1944	30	1	31	225/120	3	1890	+	1	0
15.	1944	29	0	40	170/120	4	510	+	1	0
16.	1944	44	1	26	230/140	7	1200	+	1	0
17.	1944	26	0	36	240/140	12	240	+++	4	0
18.	1944	18	0	36	170/138	0.75	270	++	4	1
19.	1944	41	5	32	185/130	4	240	++	1	0
20.	1944	38	2	38	194/120	3	2400	+	2	0
21.	1944	24	0	40	196/100	5	420	+	4	1
22.	1944	26	0	40	160/95	+	900	++	1	0
23.	1944	26	0	32	105/70	Nil	600	+++	8	0
24.	1944	32	0	40	160/100	+	360	+	6	0

* In ml. of concentrated bromethol fluid. A.R.M. = Artificial rupture of membranes

TABLE II.

s After promethol	Bromethol Dosage Initial dose*	Total No. of doses	Timing in hours H = 1st dose	Obstetrical management	Result Mother	Child	Remarks
0	6.7	1	H.	A.R.M. S.D.	A	S.B.	Antepartum; baby 3 pounds 2 ounces
0	6.3	1	H.	A.R.M. S.D.	A	A	Antepartum
0	9.5	1	H.	A.R.M. S.D.	A	D	Antepartum; baby 6 pounds 4 ounces, died aged 3 days, autopsy refused.
0	6.5	1	H.	In labour. S.D.	A	D	Antepartum; baby 7 pounds 1 ounce, died aged 8 days, no autopsy.
0	6.1	1	H.	A.R.M. Low forceps	A	A	Antepartum.
0	6.6	1	H.–	Lower segment Caesarean section.	A	D	Antepartum. Baby's weight, 2 pounds 5 ounces, died aged 24 hours.
0	5.0	2	H, H+8	A.R.M.	A	A	Intrapartum.
0	5.0	1	H.–	——	A	A	Postpartum.
0	5.5	3	H, H+5, H+10	Induction by A.R.M.	A	A	Antepartum.
0	4.4	1	H.	Breech extraction	A	A	Intrapartum and postpartum.
0	?	1	H.	——	A	A/A	Postpartum.
0	7.5	1	H.	Mid forceps	A	A	Intrapartum.
5	5.3	4	H, H+3, H+5, H+13	B.B.A.	D	A	Postpartum; see "Results", section (*f*).
0	4.7	1	H.	——	A	D/A	Postpartum; first twin 3 pounds 2 ounces, died aged 28 days.
0	7.5	4	H, H+2, H+7, H+13	Manual rotation of P.O.P mid-forceps	A	A	Intrapartum.
0	6.5	2	H, H+8	Induction by drugs	A	Abort.	Antepartum.
0	3.5	4	H, H+2, H+14, H+20	A.R.M. low forceps P.O.P.	A	S.B.	Antepartum; baby 5 pounds 4 ounces. No foetal heart heard on admission.
1	5.5	2	H, H+7	——	A	A	Postpartum.
0	6.5	1	H.	Induction by A.R.M.	A	S.B.	Antepartum; baby macerated, 2 pounds 13½ ounces.
0	6.1	2	H, H+24	Nil	A	A	Intrapartum.
1	5.5	3	H, H+3½, H+24	A.R.M. low forceps	A	A	Intrapartum; 24 hours between 4th and 5th fits.
0	5.5	1	H.	——	A	A	Postpartum.
0	6.2	1	H.	S.D.	A	D	Antepartum; baby 4 pounds.
0	5.5	4	H, H+4, H+10, H+13	Craniotomy	A	S.B.	Intrapartum; baby hydrocephalic. Six very severe seizures within 1 hour.

embranes. B.B.A. = Born before admission. S.B. = Stillborn. S.D. = Spontaneous delivery.

[*Continued overleaf*]

TABLE II (*continued*)

Case number	Date of admission	Age	Parity	Maturity on delivery (weeks)	Blood-pressure (mm. Hg.)	Urine		Oedema	Fits		Bromethol Dosage		
						Albumen g. per litre	Output in 1st 24 hours (ml.)		Before bromethol	After bromethol	Initial dose*	Total No. of doses	Timing H = 1st
25.	1945	30	7	30	170/90	4	180	+	8	0	5·5	3	H, H+
26.	1945	19	0	37	170/120	3	1710	+	1	0	6.2	2	H, H+
27.	1945	33	2	40	185/120	+++	420		3	0	6.2	4	H, H+
28.	1945	25	0	40	210/130	6	120	++	3	0	5·0	7	H, H+ H+3
29.	1945	35	3+1	33	230/150	10	360	+++	1	0	7·7	8	H, H+ H+2 H+5
30.	1945	24	0	40	180/130	2	?	++	2	0	6.1	4	H, H+
31.	1945	29	4	36	220/130	1	360	+	3	0	7·1	3	H, H+
32.	1945	37	3+1	36	160/100	2	480	++	1	0	5·5	2	H, H+
33.	1945	20	0	39	160/105	+++	270	+++	4	0	6.8	6	H, H+ H+1
34.	1945	36	0	39	160/100	6	120	+	1	0	5·5	2	H, H+
35.	1946	32	0	24	190/120	5	630	+	5	0	6.4	1	H.
36.	1946	43	1	31	210/140	+	2100	Nil	1	0	6.6	4	H, H+
37.	1946	33	0+2	40	200/140	2	360	++	1	0	5.0	3	H, H+
38.	1946	14	0	37	150/100	12	810	++	4	0	6.8	6	H, H+ H+3
39.	1946	34	1	40	260/140	10	570	Nil	1	0	6.2	1	H.
40.	1946	19	0	34	190/120	++	1200	++	2	0	3·5	2	H, H+
41.	1946	26	0	40	160/110	+	2235	+++	2	0	5.6	3	H, H+
42.	1946	26	2	46	175/105	5	2640	+	1	0	4·4	2	H+2,
43.	1946	24	0	40	170/115	0.5	?	+	1	0	5·5	1	H
44.	1946	40	0	39	140/85	+	1965	+	1	0	6.1	1	H.

* In ml. of concentrated bromethol fluid. A.R.M. = Artificial rupture of membranes.

ntinued)

Dosage Timing in hours H = 1st dose	Obstetrical management	Result Mother	Result Child	Remarks
H, H+5, H+14	Nil	A	S.B.	Antepartum and intrapartum; baby 4 pounds 14 ounces.
H, H+1	S.D.	A	D	Intrapartum; H+1 half dose. Baby 5 pounds 5 ounces; died aged 10 days. Intracranial haemorrhage. No autopsy.
H, H+2, H+4, H+7	Induction by A.R.M. S.D. twins	D	A/A	Antepartum; H+2, H+4, H+7, three-quarter doses as Avertin not well retained. Death on 5th day of puerperium. See "Results", section (*f*).
H, H+3, H+14, H+20, H+31, H+50, H+57	Induction by A.R.M., mid-forceps	A	A	Antepartum.
H, H+4, H+7, H+15, H+29, H+39, H+48, H+53.	Classical Caesarean section	A	D	Antepartum. Baby 3 pounds 7 ounces. Died aged 24 hours.
H, H+7, H+19, H+50	——	A	A	Postpartum (Mother developed but recovered from left hemiplegia).
H, H+2, H+10	Induction by A.R.M.	A	A	Antepartum.
H, H+3	——	A	A/A	Postpartum
H, H+3, H+8, H+14, H+17, H+25	Induction by A.R.M. Low cavity forceps	A	A	Antepartum, H+3, H+8 half doses.
H, H+4	(1) Assisted breech delivery (2) Int. poladic version and breech extraction	A	S.B./A	Intrapartum. First twin's cord prolapsed and pulseless on admission. Weight 5 pounds 9 ounces.
H.	Abdominal hysterotomy	A	Abort.	Antepartum.
H, H+4, H+11, H+24	Induction by A.R.M.	A	A	Antepartum.
H, H+2, H+8	A.R.M.	A	A	Intrapartum.
H, H+7, H+14, H+22, H+38, H+52	Induction A.R.M., S.D.	A	S.B.	Antepartum; baby 5 pounds.
H.	Nil, S.D.	A	A	Intrapartum.
H, H+4	A.R.M., S.D.	A	D	Antepartum: baby's weight 2 pounds 8 ounces, died aged 10 hours.
H, H+3, H+6	Lower segment Caesarean section	A	A	Antepartum.
H+2, H+4	——	A	A	Postpartum.
H	——	A	A	Postpartum.
H.	Low forceps	A	A	Intrapartum.

mbranes. S.B. = Stillborn. S.D. = Spontaneous delivery.

Technique of Administration

Dosage and Dispensing of Tri-brom-ethanol.

Initial dose. When the weight of the patient has been known, the dosage of fluid "bromethol" has been calculated on the basis of body-weight, using the mean of the recommended basal anaesthetic dosage (i.e. 0.1 ml. of concentrated bromethol solution, as dispensed by manufacturers, per kg. of body-weight) and the recommended "obstretical twilight sleep" dosage (0.75 ml. per kg.).

No attempt has been made to correct the patient's weight by deducting either the estimated weight of foetus and secundines, or the estimated weight fraction due to excessive obesity or to oedema.

Where the patient's weight has been unknown, it has been the practice to make a very rough estimate of her weight (in stones) and to calculate the dosage to the nearest stone.

The measured quantity of fluid bromethol is added to the necessary quantity of water at 40°C. to make up a final 3 per cent solution, which is then administered by slow rectal injection, after a preliminary Congo Red test to prove the absence of the acid product resulting from overheating.

When the eclampsia has developed outside hospital, it has been our practice to make up bromethol in dosage suitable for a person weighing 12 stones. A house surgeon is sent out to the patient's home with the dispensed solution in a thermos flask, having been instructed to adjust the dosage on arrival in accordance with his estimate of the patient's weight (when this is obviously less than 12 stones) by discarding either 10 ml. or 20 ml. of the solution. After such necessary adjustment, the dose is administered and 20 minutes later the patient is carried to the ambulance.

Subsequent doses. We were at first timid to repeat the dosage of bromethol, but with increasing experience we have become convinced that there is a wide margin of safety, and now do not hesitate to give repeated doses to any patient showing signs of restlessness. In general, we are quite prepared to give a second dose some 3 hours after the first. Later repeated doses are not infrequently called for, and we do not withhold them, subject to the proviso that we will not give a third or later dose within a period of less than 3 hours of the immediately preceding one; and we prefer if possible to wait even longer. Quite often patients sleep quietly for 6 to 12 hours following the second dose, and the third dose, if then given, will often enable a peaceful 24 hours to be completed. We believe that it is rarely necessary to maintain sedation for longer than this period.

Difficulties in administration. It is remarkable how seldom there is serious difficulty in administering the rectal injection, despite the fact that eclamptic patients are notoriously restless. The injection is fortunately of small bulk, and a skilful nurse can often insert the rectal catheter without much discomfort to the patient who, if her head be kept low, will then usually retain a slowly given injection.

After the withdrawal of the rectal catheter a patient will sometimes expel a small quantity of the fluid, recognised by its characteristic aromatic odour. This can generally be neglected, for the drug takes effect in some 20 minutes and, if it be retained for more than half an hour, the loss of quite large quantities has comparatively little effect in shortening the duration of action. In some cases we have given an extra half dose of the drug at once on the escape of any large quantity of fluid quickly following the initial injection.

Patients in the late second stage of labour

give difficulty owing to the pressure of the presenting part. When further sedation is indicated at this time, and natural delivery does not appear imminent, it is quite justifiable to terminate labour under general anaesthesia by operative means, after which the patient can be given the desired dose of bromethol during recovery from the anaesthetic. In passing, it may be noted that persistent relaxation of the anal sphincter following delivery under spinal anaesthesia may make it impossible for the injection to be retained.

On one occasion a patient developing eclampsia at home expelled the greater quantity of her initial dose in the ambulance on the way to hospital. On admission she was extremely restless and disorientated, and required very firm restraint. It was quite impossible to attempt a further rectal injection, but the patient was completely subdued by 0.25 g. of intravenous sodium pentothal, following which the original dose in full was administered with good effect. This woman did well.

Dangers of Bromethol

In the dosage that we have employed we have not seen any clinical evidence of liver damage, nor of any undesirable side effects other than bronchitis. None of the cases of bronchitis has been in any way alarming and the incidence does not appear to have been any higher than after other methods of management of eclampsia.

We have been fortunate in the rather short series we describe not to have encountered a case with anuria, although in several cases a more or less pronounced oliguria occurred. We do not consider that the bromethol was in any way responsible for the oliguria. We do not have information as to the possible results of giving bromethol to a patient in established anuria, although, since the drug is excreted by the kidneys, prolonged effect from a single dose might well be anticipated.

Contra-indications to Bromethol

The only contra-indication we have accepted in the present series is in respect of a single patient whose eclampsia was complicated by concealed accidental haemorrhage with marked shock (Case C in Table I).

So far as the second and subsequent doses of bromethol are concerned, we recognise the detection, by extra auscultation, of moist sounds in the respiratory passages as an indication to delay repeating the dose until the cough reflex is active. We have overriden this consideration, however, in a few cases where the clinical appearance of the patient suggested that a seizure might be imminent.

Concurrent Obstetric Management.

Antepartum eclampsia. Following the first dose of bromothol, a vaginal examination is made and, where the finger can be passed through the cervical canal, it is our practice at once to rupture the membranes artificially. Where the cervical canal cannot be penetrated by the finger, or when the cervix is unduly long or firm, we generally avoid rupturing the membranes. In such cases an endeavour is made to assess the severity of the case from the clinical findings. If the case seems to be mild we adopt a purely conservative *régime*, performing induction of labour 24 to 48 hours after the eclamptic crisis appears to have passed. When the case is judged to be a severe one, we give full consideration to the desirability of Caesarean section, which can usually be carried out successfully with local anaesthesia to supplement the bromethol. We interpolate the observation that in our very small series of cases we have treated with

bromethol we have not been in any way alarmed by the subsequent progress of the few patients delivered by Caesarean section.

Intrapartum eclampsia. Prior to the natural completion of cervical dilatation we have confined ourselves to artificial rupture of the membranes designed to accelerate labour.

In the second stage of labour we have not made any definite rule requiring operative delivery as a routine, but when eclampsia has developed for the first time towards the end of the second stage, we have usually completed vaginal delivery by operative means under general anaesthesia before commencing bromethol sedation. Apart from this we have not felt obliged to shorten the second stage except in women who were becoming restless despite sedation, or for definite mechanical indications.

The details of obstetrical management in individual cases are recorded in Table II.

Results.

(*a*) *Mortality.* The results are tabulated in Table III.

It is unfortunate that contemporaneous controls are not available from this district, but the figures for the years 1939 to 1943 are quoted for comparison.

Table III.

	Bromethol cases	Cases otherwise managed
	1943–46	1939–43
Number of patients treated	44	88
Number of babies delivered	49	82
Number of abortions	2	1
Maternal deaths	2 (4.5 per cent)	*18 (20.5 per cent)
Foetal deaths:		
Stillbirths	7	23
Neonatal deaths	8	11
Total	15 (30.6 per cent)	34 (41.5 per cent)

* Includes 8 undelivered.

(*b*) *Incidence of fits.* Apart from our earlier cases, when we were somewhat timid in repeating the dosage of bromethol, we have found it rare for fits to recur once treatment has been started. Of the total number of 44 cases, fits occurred following commencement of bromethol in 3 only. In only 1 of these was there more than a single recurrent seizure. The detail of individual cases is shown chronologically in the accompanying diagram (Fig. 1)

Again, no contemporaneous controls are available, but the incidence of fits in the 88 cases treated by sedatives other than bromethol is plotted in Fig 2, while a comparative diagram showing the percentage of patients having recurrent seizures is demonstrated in Fig. 3.

(*c*) *General effect upon patient.* Within 20 minutes of the first injection the patients became quite quiet, with tranquil breathing. The colour remained good in all cases. Respiratory embarrassment was restricted to palatal stridor. No patient was observed to vomit. Where the blood-pressure had been seriously elevated a sharp fall was invariably noted.

(*d*) *Effect upon labour.* Most cases did not show any interference with the normal course of labour, apart from a poor use of the abdominal muscles.

(*e*) *Effects upon child.* Serious apnoea was rarely observed in babies whose hearts were still beating on delivery. No case of neonatal death could be attributed to the method of sedation. We have made no attempt to provide a "corrected" figure for foetal mortality but, from the short details provided in Table II, it will be apparent that prematurity played a part, while there was one case of hydrocephalus and one of prolapse of the cord.

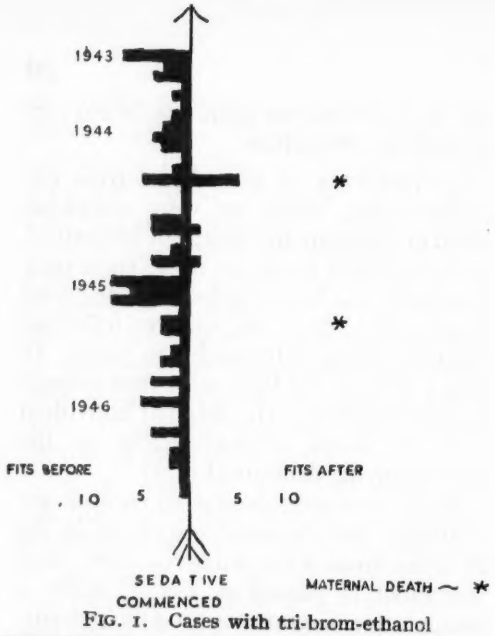

FIG. 1. Cases with tri-brom-ethanol

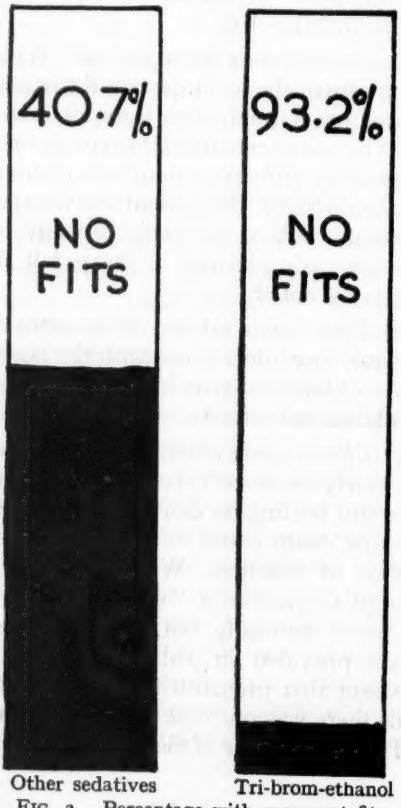

FIG. 3. Percentage with recurrent fits

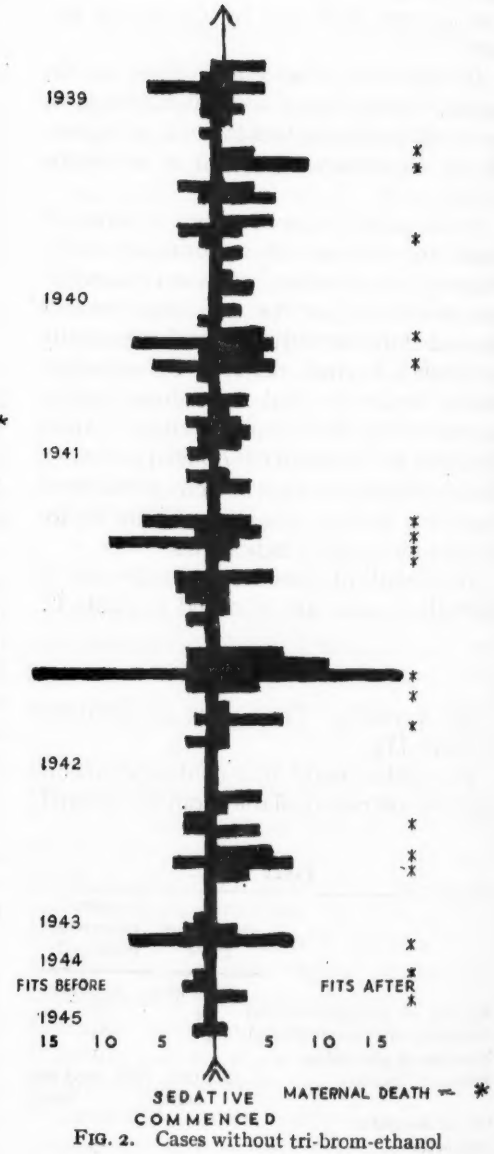

FIG. 2. Cases without tri-brom-ethanol

(f) Short notes of maternal fatalities.

CASE 13, Table II. Age 23; 2-para; unbooked; no antenatal care.

Postpartum eclampsia.

Admitted in deep coma with restlessness 7½ hours after spontaneous delivery of a living 7 pounds 4 ounces child at term. The first fit had occurred 4 hours after delivery, with a total of 6 seizures prior to admission, all described as "very severe"; temperature 98°F.; pulse-rate 136; respirations 22, with extreme stertor; blood-pressure 170/100; moderate oedema; albuminuria of 800 mg./100 ml.; urinary output uncertain owing to incontinence. Bromethol, 5.3 ml. in appropriate dilution, failed to subdue restlessness completely, and repeated doses (of 3.0 ml. only) were administered 2, 4, and 12 hours after the first, these later doses being reduced because of continuing coma with absent reflexes. There was no further restlessness after the fourth dose, but the pulse-rate became progressively more rapid, the temperature rose to 103°F. and unconsciousness persisted. Further bromethol was considered inadvisable. Twenty-four hours after admission, that is, 12 hours after the final dose of bromethol, one short fit developed. Twenty hours later 3 fits in rapid succession occurred. Lumbar puncture at this time yielded clear cerebro-spinal fluid under normal pressure. The patient died 72 hours after delivery without regaining consciousness. Venous blood taken 24 hours prior to death showed urea, 199 mg. per 100 ml. Permission for autopsy was refused. The child survived.

Obviously this was a very severe case and the fact that no fits occurred for 24 hours after commencing bromethol sedation may possibly be taken to indicate the effectiveness of the method. Whether the outcome could have been influenced favourably by continuing the treatment seems doubtful, but it may be claimed with some reason that the fatal result was not attributable to the action of the drug.

CASE 27, Table II. Age 33; 2-para; unbooked; antenatal care perfunctory.

Antepartum eclampsia.

This woman was admitted to hospital after 3 seizures. Blood-pressure 190/120; moderate oedema; heavy albuminuria. There were no fits after commencement of sedation by bromethol. Labour was induced by puncture of the membranes. Twelve hours after admission the patient was delivered spontaneously of binovular twins (1) boy, 6 pounds 13 ounces; (2) girl, 6 pounds 5 ounces. The woman recovered consciousness and the puerperium was entirely satisfactory until the fifth day, when she died very suddenly, apparently from acute heart failure (? pulmonary embolus). Permission for autopsy was refused. Both children survived.

The control of the eclampsia in this case was complete, and it seems improbable that the fatal outcome can be in any way connected with the sedative employed.

DISCUSSION.

The figures in this series in respect of maternal and foetal mortality are a distinct improvement upon those of the preceding years in the same area. They are also rather better than the average figures quoted for mortality in eclampsia in the annual reports of Scottish hospitals. However, the series is small, and there have not been synchronized control cases in the authors' hands. It would therefore be impertinent to claim that the improved figures are statistically significant.

Whilst there is no convincing evidence of diminution in the numbers or the severity of cases of eclampsia, there is an increasing tendency to transfer to hospital immediately all patients developing seizures at home or in nursing homes. The effect is undoubtedly to bring the eclamptic patient much more speedily under hospital control and, accordingly, better results are to be anticipated independently of the method of sedation adopted.

At the same time it would probably be unfair to describe the cases in the bromethol series as exclusively of a mild type. It is true that, judged by the number of fits,

they do not appear very severe; but we believe that the excellence of the sedation has been a misleading factor in this respect. As judged by the criteria of blood-pressure, albuminuria and oliguria the cases have not been mild, and our impression is that in a number of them fits would have been frequent and severe had we employed a less effective agent.

However, although we do not feel justified in claiming that management of eclampsia with bromethol will yield mortality-figures greatly differing from those obtained with other sedatives, we do strongly put forward our belief that bromethol is a very powerful anticonvulsant and is of particular value in eclampsia. The very low incidence of seizures following the institution of treatment is highly suggestive of this. The ease of handling patients under the influence of bromethol is also striking. It is quite unnecessary to resort to anaesthesia for control during catheterization or any other nursing attention, and the patients are not resentful of the changes of posture so desirable in the nursing of eclampsia. They are also tolerant of bright light, and noise does not disturb them except when the effect of the dose is beginning to wear off. They can be transported very easily under the influence of bromethol. No case has developed fits in the ambulance despite some long, rough journeys.

In our joint experience of close contact with eclamptics over the whole course of their illness we have recollection of no series of cases in which we were less anxious about the patients, and in which the patients were easier to handle.

We have come to have such great confidence in the effects of bromethol that we are now disposed to take a much more conservative view of the management of pre-eclampsia. We believe that in bromethol we have a sedative agent which enables us to persevere with conservative treatment, even in the presence of urgent prodromal symptoms of eclampsia, since we can confidently expect to control any seizures which do actually develop. We realise that the severity of eclampsia is controlled by factors additional to the number of fits and that it is unlikely that these factors will be influenced at all favourably by bromethol, possibly the reverse. Nevertheless, this trust in our sedative agent has given us added confidence in the handling of these difficult cases.

In parenthesis, we think it permissible to refer to the fact that in many cases of severe pre-eclampsia we have used bromethol in the initial treatment and during labour, and that no case has developed fits when under its influence. We have also used bromethol from time to time as an analgesic in normal labour, but are not so favourably impressed with it in this field. Sedation has seemed to us more difficult to achieve than in the eclamptic. We do not wish to decry bromethol in this respect, but in our hands it has proved erratic.

Summary

1. Details of a series of 44 eclamptics from South-West Scotland are given.

2. All cases recorded were managed by sedative treatment using rectal tri-bromethanol (Avertin, Bromethol).

3. Attention is drawn to the favourable course of these cases with regard to the control of fits.

4. Maternal mortality in cases so treated was 4.5 per cent.

5. Foetal mortality was 30.6 per cent.

Acknowledgments

We wish to thank the members of our nursing staffs, without whose skill the results would have been even less favourable than

those obtained. We are much indebted to Messrs. Bayer and Co., Messrs. British Drug Houses Ltd., and Messrs. Burroughs Wellcome and Co., for help with references to the literature.

References

Benthin, W. (1927): *Dtsch. med. Wschr.*, **53**, 955.
Boyce, F. F. and McFetridge, E. M. (1935): *New Orleans med. surg. J.*, **87**, 825.
Carré, J. and Gellé, P. (1938): *Curr. Res. Anesth.*, **4**, 55.
Coghlan, C. (1931): *Med. J. Aust.*, **1**, 737.
Cole, L. (1935): *Lancet*, **2**, 246.
Cole, L. (1936): *Brit. med. J.*, **1**, 1191.
Cole, L. (1942): *Brit. med. J.*, **2**, 550.
Conrad, G. (1927): *Zbl. Gynäk.*, **51**, 2222.
Freeman, E. T. (1936): *Brit. med. J.*, **1**, 552.
Gellé, P. (1939): *Gynéc. et Obstét.*, **39**, 285.
Huntingdon, R. W. (1931): *Yale J. Biol. Med.*, **11**, 207.
Läwen, D. (1927): *Zbl. Chir.*, **54**, 2370.
Läwen, D. (1928): *Zbl. Chir.*, **55**, 194.
Miller, N. F. (1944): *J. Iowa St. med. Soc.*, **34**, 457.
Mitchell, H. S. (1935): *Canad. med. Ass. J.*, **32**, 415.
Morrison, G. H. (1931): *Prescriber*, 38.
Pierce, J. M. (1931): *J. Mich. med. Soc.*, **30**, 691.
Sartorius, K. (1933): *S. Afr. med. J.*, **7**, 694.
Sennewald (1928): *Zbl. Gynäk.*, **52**, 155.
Shiplay, A. M. and Cairns C. (1930): *Trans. Sect. Surg., Amer. med. Ass.*, 54.
Whitaker, C. W. (1933): *West. J. Surg.*, **41**, 347.

The Excretion of Drugs in Human Milk—A Review

BY

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FROM time to time information is sought with regard to the excretion of drugs in human milk. No comprehensive account appears in the literature. There are in the main but scanty isolated reports. Many of the older statements are not based on accurate scientific or chemical investigation and are valueless. Only occasional investigations have been made owing to the difficulties involved. In recent years more thorough studies have been made with regard to a few drugs, especially the sulphonamides. Here chemical analyses have been made on a fair number of lactating women, and often correlated with other findings such as the corresponding levels in the blood.

In the following review the medical literature in the English language has mainly been consulted. It will be noted that there is no information at all on the excretion of many substances used in therapeutics, and details about others on which reports have been made are very inadequate. There is still scope for research on this subject, which will increase with the rapid introduction of new therapeutic agents.

One of the earliest reviews of this subject was made by Reed (1908) many of whose observations still hold good to-day. The fact that it is practically never necessary to remove the child from the breast when the mother is receiving drug therapy is borne out by the rarity of cases of untoward reactions reported in the literature. Another important point that still holds is that it is rarely if ever desirable to treat a child with drugs given to the mother. From the clinical and qualitative chemical evidence at that time Reed concluded that alcohol, opium, chloroform, ether, thyroid, and lead are to be used with care, and that atropine, antipyrine (phenazone), phenacetin, chloral, arsenic, bismuth, mercury, copper, castor oil, senna, quinine, bromides, iodides, salicylic acid, and copaiba, pass into the milk in small quantities. An almost identical list is given by Stander (1941).

In the account presented here the reports since 1908 have been studied. The vitamin content of human milk has not been considered.

CENTRAL NERVOUS DEPRESSANTS.

Alcohol. The milk may contain a small amount of alcohol if large quantities are ingested, but not with ordinary doses (Sollmann, 1942). While the maximum amount excreted has been regarded as too small to affect sucklings, a case of poisoning in a breast fed infant 8 days old has been reported (Bisdom, 1937). The mother consumed 750 g. of port. The child was in deep sleep from which it could not be wakened. Alcohol was found in the blood of the mother and child.

Chloroform. According to Scanzoni, quoted by Reed (1908), a newborn child, whose mother had been given chloroform

for after-pains, stopped suckling after a short while on the breast and remained in a deep sleep for 8 hours.

Barbiturates. Excretion of barbiturate into breast milk has been demonstrated, but the amount is generally too small to affect the infant. Kwit and Hatcher (1935) could find no evidence of barbitone 6 hours after the administration of doses of 650 mg. (10 gr.). These authors doubted whether in a report made by Frensdorf (1926) phenobarbitone was the cause of depression in an infant whose mother had taken 0.8 g. of the drug in 3 days.

Tyson *et al.* (1938) found the amount excreted is somewhat greater when the barbiturate is given in a single dose than when it is distributed.

A small amount of barbiturate was found in the milk by Mayo and Schlicke (1942) after an injection of 1125 mg. pentothal sodium; the concentration was higher than in the blood.

Chloretone. Blanner (1919) stated that this drug is found in the milk only with continuous administrations of very large doses. With doses of 5 to 20 gr. he found no trace even with doses repeated several times. No antigalactogogic effect was observed such as can be produced with relatively larger doses in lactating dogs.

Bromides. This is well known as a possible cause of a skin eruption in infants; for example, Van der Bogert (1921) found "more than traces" in the milk which caused a papulopustular eruption.

Kwit and Hatcher (1935) found sodium bromide in the milk of mothers given 1 g. 5 times daily for 3 days; in one specimen of 120 ml. there were 8 mg. of the drug.

Tyson *et al.* (1938) found that the amount excreted may have a sedative effect on the infant.

Morphine. Talbot (1914) stated that morphine had not yet been found in human milk. Terwilliger and Hatcher (1934) found no alkaloid in the milk of an addict taking 20 gr. of morphine sulphate daily, while in a normal woman given 16 mg. of this drug a trace may have been present in the milk 7½ hours later. In another investigation no alkaloid could be detected with certainty by Kwit and Hatcher (1935) 4 hours after subcutaneous injection of 16 mg. of morphine sulphate.

Codeine. None of the alkaloid was recovered 4 hours after single doses of 65 mg. nor after 6 doses of 32 mg. given every 4 hours (Kwit and Hatcher, 1935).

Autonomic Drugs.

Atropine. Paterson and Smith (1938) state that atropine is not excreted in the milk. It is well known that belladonna or its alkaloid atropine markedly diminish the milk flow (Stander, 1941), and the drug transmitted through the milk may affect the child.

Hyoscine. This alkaloid is rapidly destroyed in the tissues and only minute traces appear in the milk; thus there should be no danger in prescribing it for a nursing mother, for example when used to prevent seasickness (*Brit. Med. J.*, 1946).

Nicotine. Tobacco is being smoked by women on an increasingly large scale. The problems in connexion with this habit that have been investigated are (*a*) whether the important constituent, nicotine, is excreted in the breast milk, (*b*) whether the infant can be affected by nicotine in the milk, and (*c*) whether lactation itself is affected.

Hatcher and Crosby (1928) found that large doses suppress the secretion of milk in the cat and the cow. In one woman who smoked 20 to 25 cigarettes daily for 6 days the milk secretion became reduced; using the frog method they found less than 0.015 mg. of the alkaloid in some milk (about 26 ml.) collected after 7 cigarettes

had been smoked in 2 hours. Chiasson (1929) found good lactation in French families where the women were regular pipe smokers.

Emanuel (1931) in a study on 10 patients found nicotine in the milk, sometimes 1 or 2 hours after smoking, but the main excretion was after 4 or 5 hours, and in some cases was still demonstrable 7 to 8 hours after smoking. Leech segments were used for estimating the nicotine and by this method a maximum of 0.03 mg. per litre of milk was found after the smoking of 7 to 15 cigarettes, an amount below the toxic threshold.

Thompson (1933) also found nicotine in breast milk. He stated that he had not observed a patient smoking 8 or more cigarettes daily whose lactation was adequate at 3 months after delivery.

Nicotine intoxication in factories or from excessive smoking may affect the mother and also the child.

Poisoning has occurred in a breast fed infant 6 weeks old. The mother smoked 20 cigarettes a day and her milk contained nicotine. The symptoms were restlessness, insomnia, "spastic" vomiting, diarrhoea, rapid pulse, and circulatory disturbances; recovery occurred with symptomatic treatment (Bisdom, 1937).

In a recent study Perlman, Dannenberg and Sokoloff (1942) using *Daphnia magna*, a fresh water crustacean, as test organism, found nicotine in every specimen of milk obtained from 55 mothers who smoked varying numbers of cigarettes, from 1 up to 20 or more over a 12-hour period. By this method higher values, average 0.116 to 0.5 mg. per litre of milk, were obtained than in the case of Hatcher and Crosby (1928) and Emanuel (1931) mentioned above. They concluded that lactation and the nursling were little if at all affected by the nicotine, due to the development of tolerance for the drugs, especially as all the mothers had smoked before.

Purgatives.

Phenolphthalein. None of the drug was detected after administration of a dose of 90 mg. (1½ gr.) (Kwit and Hatcher, 1935).

According to Fantus and Dyniewicz (1936) no free phenolphthalein is excreted in the milk within 24 hours or more of taking large doses (0.2 to 0.8 g.) of phenolphthalein. Minute quantities of conjugated phenolphthalein may be found. No obvious effect on the bowel movements occurred in the infants of mothers taking phenolphthalein.

Emodin. This is the active constituent of senna, cascara, rhubarb, aloes. A certain amount is absorbed and may produce purgation in the suckling (Sollmann, 1942). Tyson *et al.* (1937) found no evidence of phenolphthalein, calomel, senna, or rhubarb on chemical analysis. Aloin was transmitted in too small amount for laxative action in the child. Cascara gave both chemical and clinical evidence of transmission.

Antimicrobial Agents.

Sulphonamides. Sulphanilamide may be found in the milk in both the free and the conjugated form and is present for days after administration has ceased. In an investigation on 20 subjects Adair, Hesseltine, and Hac (1938) found 3.76 to 13.67 mg. sulphanilamide in the milk after doses of 2 g. and 11.77 to 54 mg. after doses of 4 g., a variation of 0.006 to 0.016 and from 0.019 to 0.04 mg. per ml. The drug was present in both free and acetylated forms, and the level was much higher in the milk than in the blood.

In a later study Hac, Adair, and Hesseltine (1939) gave 25 normal lactating women

2 to 5 g. of the drug in 6 doses daily for 3 days. The drug was still found in small amount 48 hours after administration was stopped. The percentage of drug excreted as the conjugated acetyl form varied from 35.1 to 83.9. The total amount excreted during 5 days was never greater than 0.23 g. or 1.6 per cent of the amount ingested, too small to be dangerous to the infant.

Stewart and Pratt (1938) found that after 2 g. of sulphanilamide the concentration of free drug in the milk corresponded to levels in the blood (2 to 4 mg. per 100 ml.), and after 4 g. doses the concentration was equal to or slightly higher than the blood level of 4 to 7 mg. per 100 ml. No toxic effects occurred in babies drinking the milk; traces of the drug were present in the blood and urine of the baby.

Pinto (1938) found the concentration of sulphanilamide after a single large dose of 4 g. followed the concentration in the blood, but lagged behind by a few hours. Hepburn, Paxson, and Rogers (1938) gave a daily dose of sulphanilamide of 1.6 g. (0.3 g. every 4 hours) and found the free drug in the milk 24 hours later in a concentration between 0.55 and 2.17 mg. per 100 ml. Where the mothers received sulphanilamide for several additional days, the drug was found in the urine of the infants in concentration varying from 0.19 to 1.4 mg. per 100 ml. In a later investigation these workers (Hepburn, Paxson and Rogers, 1942) found 0.5 to 2.7 mg. per 100 ml. milk of the free form and 0 to 7.2 of the conjugated form, total 1.9 to 9.4; in the urine of infants obtained at the same time there was 0.5 to 2.7 of free sulphanilamide, 0.9 to 21.7 of conjugated form, with a total of 1.3 to 25 mg. per 100 ml.

Foster (1939) reported the excretion of sulphanilamide in the milk.

Aguirre and collaborators (1942) have determined the excretion of various sulphonamide compounds in milk.

When sulphathiazole was given in daily doses of 3 g. Rieben and Druey (1942) found 0.5 to 1.5 mg. of the free form per 100 ml. milk, and after doses of 6 g. daily 1 to 2 mg., the corresponding blood levels being 2 to 3 times this amount. The infant received not more than a total daily amount of 4 mg.

Penicillin. Greene, Burkhart, and Hobby (1946) found penicillin in the breast milk in small amounts (0.015 to 0.06 unit per ml.) the blood levels ranging from 0.112 to 1.92 units per ml. following intramuscular injection of doses of 100,000 units.

Mandelic acid. In a study on 6 mothers (and their infants) Berger (1941) found that when 12 g. mandelic acid are given daily from the first day of delivery and with the daily fluid intake restricted to 1,200 ml. the amount in samples of the breast milk varied considerably. The estimated average amount of the drug excreted in 24 hours was 0.2726 g. Thus the infants never get a dangerous amount of the drug.

Hexamine. According to Sollmann (1942) this substance has been found in the milk; the highest concentration was reached after an hour .

Arsphenamine (*Salvarsan*). According to Paterson and Smith (1938) salvarsan is not excreted in the milk.

Other Substances.

Iodide. This was found only in very small amount by Kwit and Hatcher (1935) after total doses of 3.6 (325 mg. were given 3 times daily) and 4.6 (650 mg. 3 times daily) grammes of the potassium salt.

After a dose of 0.6 g. (10 gr.) of potassium iodide, Maurer and Ducrue (1928) found about 68 mg. or 15 per cent of the dose in the milk in 3 days. According to

Sollmann (1942) milk normally contains some iodide, 0.02 to 0.03 mg. per litre.

Fluoride. Small quantities have been found in milk (Sollmann, 1942). This is of interest in view of the effects of fluorine on bone and tooth enamel.

Quinine. Only traces were found in milk by Terwilliger and Hatcher (1934) even after doses of 640 mg. (10 gr.).

Salicylic acid. This could be detected even after giving 10 gr. of sodium salicylate (Kwit and Hatcher, 1935).

Ergot alkaloids. These were found in the milk by Fomina (1934); some infants showed clinical signs of intoxication.

Caffeine. Traces of this substance or a derivative were found in the milk of coffee or tea drinkers (Irvin, 1926).

Schilf and Wohinz (1928) recovered about 1 per cent of the caffeine in milk drawn 6 hours after coffee had been taken.

Radio-active sodium. This substance has been recovered in the milk within 20 minutes of administration, with a maximum concentration in about 2 hours, the subsequent secretion falling slowly with sodium still recoverable after 96 hours (Pommerenke and Hahn, 1943).

Colchicum. According to Garrod *et al.* (1929) this substance may pass into the milk.

Carotene: Consumption of several carrots daily caused carotenoderma (carotenaemia) in a mother and her suckling of 6 months. The yellowness of the infant's skin disappeared when the breast feeding was stopped (Thomson, 1943).

REFERENCES.

Adair, F. L., Hesseltine, H. C., and Hac, L. R. (1938): *J. Amer. med. Ass.*, **111**, 766.

Aguirre, R. C. *et al.* (1942): *An. Soc. Pueric. Buenos Aires*, **8**, 1. (*Abstr. J. Amer. med. Ass.*, 1942, **120**, 485).

Berger, H. (1941): *Amer. J. Dis. Child.*, **61**, 256.

Bisdom, C. J. W. (1937): *Maandschr. Kindergeneesk.*, **6**, 299. (Abstr. *J. Amer. med. Ass.*, 1937, **109**, 178).

Blanner, J. E. (1919): *J. Lab. clin. Med.*, **4**, 501.

British Medical Journal (1946): *Brit. med. J.*, **1**, 720.

Chiasson, M. J. (1929): Quoted by Johnson, W. M. (1929): *J. Amer. med. Ass.*, **93**, 1909.

Emanuel, W. (1931): *Z. Kinderheilk.*, **52**, 41.

Fantus, B. and Dyniewicz, J. M. (1936): *Amer. J. dig. Dis.*, **3**, 184.

Fomina, P. I. (1934): *Arch. Gynäk.*, **157**, 275. (Abstr. *Biol. Abstr.*, 1935, **9**, 2034).

Foster, F. P. (1939): *Proc. Mayo Clin.*, **14**, 153.

Frensdorf (1926): *Münch. med. Wschr.*, **73**, 322.

Garrod, A. E., *et al.* (1929): *Diseases of Children.* London.

Greene, H. J., Burkhart, B., and Hobby, G. L. (1946): *Amer. J. Obstet. Gynec*, **51**, 732.

Hac, L. R., Adair, F. L., and Hesseltine, H. C. (1939): *Amer. J. Obstet. Gynec.*, **38**, 57.

Hatcher, R. A., and Crosby, H. (1928): *J. Pharm. exp. Ther.*, **32**, 1.

Hepburn, J. S., Paxson, N. F., and Rogers, A. N. (1938): *J. biol. Chem.*, **123**, 54.

Hepburn, J. S., Paxson, N. F., and Rogers, A. N. (1942): *Arch. Pediat.*, **59**, 413.

Irvin, R. R. (1926): *Med. J. Rec.*, **124**, 37 (Abstr. *Biol. Abstr.* (1928): **2**, 1028).

Kwit, N. T. and Hatcher, R. A. (1935): *Amer. J. Dis. Child.*, **49**, 900.

Maurer, E., and Ducrue, H. (1928): *Münch. med. Wschr.*, **75**, 249. (Abstr. *Biol. Abstr.*, 1930, **4**, 775.)

Mayo, C. W., and Schlicke, C. P. (1942): *Proc. Mayo. Clin.*, **17**, 87.

Paterson, D., and Smith, J. F. (1938): *Modern methods of feeding in infancy and childhood.* London.

Perlman, H. H., Dannenberg, A. M., and Sokoloff, N. (1942): *J. Amer. med. Ass.*, **120**, 1003.

Pinto, S. S. (1938): *J. Amer. med. Ass.*, **111**, 1914.

Pommerenke, W. T., and Hahn, P. F. (1943): *Proc. Soc. exp. Biol. N.Y.*, **52**, 223.

Reed, C. B. (1908): *Surg., Gynec. Obstet.*, **6**, 514.

Rieben, G., and Druey, J. (1942): *Schweiz. med. Wschr.*, **72**, 1376.

Schilf, E., and Wohinz, R. (1928): *Arch. Gynäk.*, **134**, 201.

Sollmann, T. (1942): *Manual of Pharmacology*, Philadelphia.

Stander, H. J. (1941): Williams' *Obstetrics*, 8th ed., New York.

Stewart, H. L., and Pratt, J. B. (1938): *J. Amer. med. Assoc.*, **111**, 1456.

Talbot, F. B. (1914): *Amer. J. Dis. Child.*, **7**, 445.

Terwilliger, W. G., and Hatcher, R. A. (1934): *Surg. Gynec. Obstet.*, **58**, 823.

Thompson, W. B. (1933): *Amer. J. Obstet. Gynec.*, **26**, 662.

Thomson, M. L. (1943): *Arch. Dis. Childh.*, **18**, 112.

Tyson, R. M., Shrader, E. A., and Perlman, H. H. (1937): *J. Pediat.*, **11**, 824.

Tyson, R. M., Shrader, E. A., and Perlman, H. H. (1938): *J. Pediat.*, **13**, 86, 91.

Van der Bogert, F. (1921): *Amer. J. Dis. Child.*, **21**, 167.

Calcium and Phosphorus Metabolism in Pregnancy
(A Survey under War and Post-war Conditions)

First Communication on the Temperamental and Emotional Factor

BY

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The present communication deals with a further 17 women, cases 37 to 53, whose calcium intake and output figures are shown in Table I.

The reader is referred to the two previous papers (Obermer, 1946a; 1946b) on this subject for (*a*) an outline of the investigation as a whole, its scope and objectives; (*b*) references which cover most of the published work on calcium and phosphorus metabolism during pregnancy, as well as most of the Calciferol literature; (*c*) calcium intake and output figures of a group of control women (Group I), a group of women given a supplement of calcium phosphate (Group II) and a further group given the same doses of calcium phosphate together with large amounts of Calciferol (Group III).

The figures given in Table I are the calcium intake and output figures of cases 37 to 53, who were on a self-chosen diet, had no calcium phosphate supplement, but were given Calciferol in the following dosage:

Cases 36 and 37.
800 units of D_2 per day throughout pregnancy. (In the form of " Government Capsules ", as distributed at health centres and antenatal departments. Each capsule also contained 97 mg. of calcium and 50 mg. of phosphorus—quantities so small that they can be disregarded as supplements.)

Cases 39 to 41.
1,000 units first 6 months; 2,000 units last 3 months (in the form of Radiostol liquid).

Cases 42 and 43.
3,000 units for first 6 months; 6,000 units for last 3 months.

Cases 44 to 46.
3,000 units up to end of 5th month; 6,000 units 6th and 7th months; 9,000 units 8th month onwards.

Cases 47 and 48.
9,000 units first 6 months; 18,000 units last 3 months.

Cases 49 and 50.
9,000 units up to end of 5th month; 18,000 units 6th and 7th months; 27,000 units 8th month onwards.

Cases 51 to 53.
18,000 units up to end of 5th month; 27,000 units 6th and 7th months; 36,000 units 8th month onwards.

(Cases 43 to 53 had their supplement in the form of Radiostol pellets—3,000 units each.)

Comparison of Calcium and Phosphorus Balances.

The figures for all 4 groups are given in Tables II and III.

If these tables are compared with the similar tables in a previous paper (Obermer, 1946b) it will be seen that a further 16 control or Group I balances have been added. These have been taken from Section 1 of Table I in the present paper and represent the preliminary investigations (before Calciferol supplements were given) together with 3 balances during later stages of pregnancy, when no Calciferol supplements had been taken for

TABLE I.

Tabulation of Calcium Intake and Output Figures.

(The figures on each line represent the findings of a 48-hour period in terms of grammes of calcium element).

Date	Week of pregnancy	Case No.	Calcium intake: Milk	Cheese	Other foods	Sup.	Total	Calcium in blood	Calcium in urine	Calcium in faeces	Total calcium output	Calcium balance
Section 1												
1. 2.1945	18	37	1.93	Nil	0.37	Nil	2.30	10.7	0.77	0.62	1.39	+0.91
7. 5.1945	30		1.94	Nil	0.34	Nil	2.28	9.7	0.48	0.56	1.04	+1.24
8. 7.1945	24	39	1.51	Nil	0.37	Nil	1.88	10.0	0.36	2.80	3.16	−1.28
10.10.1945	38		1.75	0.24	0.30	Nil	2.29	—	1.05	1.82	2.87	−0.58
21. 7.1945	14	40	2.12	Nil	0.73	Nil	2.83	12.1	1.37	1.12	2.49	+0.36
23.10.1945	9	41	1.28	Nil	0.59	Nil	1.87	10.2	0.87	4.60	5.47	−3.60
6. 9.1945	12	42	0.92	Nil	0.21	Nil	1.13	11.4	0.73	1.72	2.45	−1.32
14. 9.1945	9	43	0.61	0.36	0.35	Nil	1.32	10.0	0.34	1.30	1.64	−0.32
4.10.1945	14	44	1.10	0.12	0.79	Nil	2.01	9.8	1.10	3.50	4.60	−2.59
13.10.1945	9	45	1.34	Nil	0.49	Nil	1.83	11.0	0.78	2.85	3.63	−1.80
19.12.1944	15	47	2.00	Nil	0.64	Nil	2.64	10.9	0.89	2.06	2.95	−0.31
14. 5.1945	10	49	1.16	Nil	0.59	Nil	1.75	10.0	0.72	2.25	2.97	−1.22
9. 6.1945	21	50	1.22	0.12	0.58	Nil	1.92	10.4	0.65	1.64	2.29	−0.37
8.11.1945	9	51	1.15	0.12	0.45	Nil	1.72	9.8	0.79	1.62	2.41	−0.69
22. 1.1946	8	53	1.09	0.61	0.42	Nil	2.12	9.7	0.53	0.72	1.25	+0.87
16. 8.1946	39		2.22	0.32	0.33	Nil	2.87	—	0.74	3.20	3.94	−1.07
Section 2												
22. 3.1945	24	37	1.76	Nil	0.45	0.19	2.41	11.0	0.45	1.30	1.75	+0.66
16. 6.1945	36		0.85	0.12	0.64	0.19	1.80	9.9	0.44	2.16	2.60	−0.80
13. 6.1945	17	38	1.76	Nil	0.49	0.19	2.44	9.7	0.40	0.93	1.33	+1.11
26. 7.1945	23		1.28	0.48	0.40	0.19	2.35	9.4	0.64	1.53	2.17	+0.18
12. 9.1945	30		1.57	0.48	0.54	0.19	2.78	10.5	0.83	2.07	2.90	−0.12
25. 8.1945	31	39	1.44	0.12	0.31	Nil	1.87	10.2	0.97	1.68	2.65	−0.78
24.10.1945	40		1.77	Nil	0.36	Nil	2.13	—	0.76	1.00	1.76	+0.37
5. 9.1945	20	40	1.34	Nil	0.47	Nil	1.81	11.4	0.63	2.20	2.83	−1.02
12.10.1945	26		1.15	Nil	0.66	Nil	1.81	11.9	0.49	2.09	2.58	−0.77
29.11.1945	31		0.58	0.27	0.72	Nil	1.57	10.1	0.63	1.25	1.88	−0.31
6.12.1945	15	41	1.24	0.69	0.71	Nil	2.64	9.8	0.78	2.23	3.01	−0.37
24. 1.1946	21		1.60	0.69	0.60	Nil	2.89	9.6	0.92	2.05	2.97	−0.08
8. 3.1946	27		2.36	0.97	0.45	Nil	3.78	10.6	1.03	3.94	4.97	−1.18
16.10.1945	18	42	1.62	0.20	0.23	Nil	2.05	11.0	0.45	0.97	1.42	+0.63
29.11.1945	24		0.90	Nil	0.34	Nil	1.24	9.7	0.42	0.80	1.22	+0.02
15. 1.1946	31		1.22	Nil	0.21	Nil	1.43	10.0	0.56	0.80	1.36	+0.07
19.10.1945	15	43	0.58	Nil	0.63	Nil	1.21	9.6	0.39	1.70	2.09	−0.78
29.11.1945	21		0.53	0.36	0.59	Nil	1.48	10.4	0.37	2.40	2.77	−1.29
15. 1.1946	28		1.48	Nil	0.76	Nil	2.24	10.7	0.25	1.96	2.21	+0.03
26. 2.1946	34		0.68	Nil	0.87	Nil	1.55	10.6	0.32	2.00	2.32	−0.77

[*Continued overleaf*

TABLE I—*Section 2 [continued]*

Date	Week of pregnancy	Case No.	Calcium intake					Calcium in blood	Calcium in urine	Calcium in faeces	Total calcium output	Calcium balance
			Milk	Cheese	Other foods	Sup.	Total					
27.11.1945	21	44	1.68	Nil	0.95	Nil	2.63	10.2	0.78	4.30	5.08	−2.45
17. 1.1946	28		1.52	0.27	0.67	Nil	2.46	10.4	0.72	1.15	1.87	+0.59
28.11.1945	15	45	1.52	0.27	0.53	Nil	2.32	9.7	0.79	2.60	3.39	−1.07
18. 1.1946	22		1.64	0.40	0.42	Nil	2.46	10.6	0.89	2.50	3.39	−0.93
28. 2.1946	28		1.81	Nil	0.41	Nil	2.22	9.8	1.36	5.39	6.75	−4.53
12. 4.1946	34		2.36	0.56	0.51	Nil	3.43	10.4	0.57	5.15	5.72	−2.29
24.10.1945	11	46	1.70	0.20	0.27	0.19	2.35	10.8	0.82	1.31	2.13	+0.23
7.12.1945	17		1.29	0.12	0.37	0.19	1.97	10.4	0.69	2.50	3.19	−1.22
29. 1.1946	23		1.34	0.44	0.51	0.19	2.48	—	0.47	2.26	2.73	−0.25
6. 3.1946	29		1.86	0.12	0.62	0.19	2.79	—	0.93	1.96	2.89	−1.00
13. 4.1946	34		1.34	Nil	0.70	0.19	2.23	—	0.64	2.15	2.79	−0.56
27. 1.1945	21	47	1.72	Nil	0.66	0.29	2.67	11.0	0.81	1.78	2.59	+0.08
12. 3.1945	27		2.04	Nil	0.52	0.19	2.75	11.5	0.58	3.00	3.58	−0.83
23. 4.1945	33		2.32	0.20	0.77	0.19	3.48	10.8	0.76	1.80	2.56	+0.92
28. 5.1945	38		2.00	Nil	0.45	0.19	2.64	11.0	0.81	2.00	2.81	−0.17
9. 2.1945	8	48	0.81	0.40	0.90	0.19	2.30	10.9	0.70	1.71	2.41	−0.11
23. 3.1945	14		2.05	0.42	0.67	0.19	3.33	11.4	0.80	3.56	4.36	−1.03
8. 5.1945	20		1.87	0.36	0.51	0.19	2.93	10.2	0.52	3.65	4.17	−1.24
16. 6.1945	26		2.40	0.29	0.54	0.19	3.42	10.2	0.63	2.55	3.18	+0.24
1. 8.1945	32		2.01	0.27	0.57	0.19	3.04	10.2	0.36	1.73	2.09	+0.95
3. 9.1945	38		1.20	0.40	0.52	0.19	2.31	10.6	0.96	1.46	2.42	−0.11
21. 6.1945	16	49	1.46	Nil	0.45	Nil	1.91	10.8	0.66	1.22	1.88	+0.13
11. 8.1945	24		1.12	Nil	0.43	Nil	1.55	10.0	0.77	1.12	1.89	−0.34
21. 9.1945	30		0.99	0.27	0.41	Nil	1.67	10.4	1.06	0.83	1.89	−0.22
3.11.1945	36		1.33	0.12	0.28	Nil	1.73	10.6	0.77	1.21	1.98	−0.25
21. 7.1945	27	50	1.32	Nil	0.55	Nil	1.87	10.8	0.83	0.82	1.65	+0.22
4. 9.1945	33		1.02	0.27	0.46	Nil	1.75	9.9	0.62	1.04	1.66	+0.09
2.10.1945	39		1.16	Nil	0.34	Nil	1.50	8.9	0.92	1.35	2.27	−0.77
14.12.1945	14	51	1.57	0.27	0.60	Nil	2.44	10.0	1.01	2.20	3.21	−0.77
12. 2.1946	22		1.12	0.56	0.56	Nil	2.24	10.0	0.76	1.29	2.05	+0.19
18. 3.1946	27		1.30	0.49	0.60	Nil	2.39	10.0	0.48	0.45	0.93	+1.46
7. 5.1946	34		1.88	0.44	1.60	Nil	3.92	10.0	0.83	1.79	2.62	+1.30
6. 6.1946	38		1.84	Nil	0.74	Nil	2.58	10.0	0.78	2.90	3.68	−1.10
8. 1.1946	8	52	0.83	0.73	0.64	0.19	2.39	10.5	0.24	2.28	2.52	−1.13
22. 2.1946	14		0.86	0.40	0.83	0.19	2.28	9.8	0.71	2.12	2.83	−0.55
24. 4.1946	22		2.43	0.45	0.92	0.19	3.99	10.0	0.55	3.60	4.15	−0.16
4. 6.1946	28		1.66	0.20	0.53	0.19	2.58	10.0	0.64	3.30	3.94	−1.36
8. 7.1946	33		1.06	0.49	0.31	0.19	2.05	—	0.57	3.06	3.63	−1.58
6. 8.1946	37		1.42	0.25	0.45	0.19	2.31	10.8	0.45	1.84	2.29	+0.02
5. 3.1946	14	53	1.75	0.97	0.44	Nil	3.16	9.9	0.99	5.40	6.39	−3.23
16. 4.1946	20		1.92	0.40	0.50	Nil	2.82	9.3	0.75	3.20	3.95	−1.13
28. 5.1946	28		1.29	0.32	0.39	Nil	2.00	11.0	0.65	2.40	3.05	−1.05
16. 7.1946	35		1.26	0.44	0.42	Nil	2.12	9.9	0.74	2.25	2.99	−0.87

TABLE II.

Calcium Balances.

	Group I	Group II	Group III	Group IV
Number of balances	84	36	44	63
Percentage negative balances	80	44	22.5	54
Percentage equilibrium	7	3	4.5	27
Percentage positive balances	13	53	73	19

more than a week, as their supplies had run out, owing to a miscalculation. The 63 balances analyzed in Group IV represent all the figures given in Section 2 of Table I. It was considered desirable to lump all these balances together, in spite of the varying dosage of Calciferol, to see whether a definite influence of Calciferol could be demonstrated.

TABLE III.

Phosphorus Balances.

	Group I	Group II	Group III	Group IV
Number of balances	84	36	44	63
Percentage negative balances	40	42	16	41
Percentage equilibrium	12	11	7	21
Percentage positive balances	48	47	77	38

Group I—Controls.
Group II—Calcium phosphate.
Group III—Calcium phosphate plus Calciferol.
Group IV—Progressive doses of Calciferol only.

As the calcium intakes in Group I and Group IV cases were similar any marked increase in the percentage of Group IV positive balances, as compared with Group I, could be considered proof, or at any rate an indication, that Calciferol by itself does have a definite effect on calcium and phosphorus metabolism during pregnancy. There is, in fact, no statistically significant increase in the percentage of positive calcium balances, though there is a definite decrease in the percentage of negative balances. The increase in percentage of equilibria might be considered to reflect Calciferol action, were the numbers sufficient to be statistically significant. This is hardly the case.

The figures in Table III are somewhat surprising, as the increase in the percentage of positive phosphorus balances in Group III was even more striking than the increase in positive calcium balances as shown in Table II. The Group IV figures show no decrease in the percentage of negative phosphorus balances, though there is an increase in the percentage of equilibria, parallel to the increase of calcium equilibria in Table II.

In an attempt to assess the influence of the Calciferol factor the balance figures taken from Section 2 of Table I were further analyzed out in relation to calcium intake levels, and are given in Table IV.

When these figures are compared with the corresponding figures (printed in brackets) from Table IV in a previous paper

TABLE IV.

Correlation between Calcium Intake Levels and Calcium Balances.
(Analysis of Group IV Cases—Calciferol only).

Intake per 24 hours	No. of balances	Balance positive	Equilibrium	Balance negative	Percentage negative balances
Below 1 g.	18 (27)	1 (?1)	4 (1)	13 (25)	60 (93)
Between 1.1–1.5 g.	37 (20)	3 (4)	1 (0)	4 (8)	50 (67)
Between 1.6–2.0 g.	8 (12)	8 (2)	12 (1)	17 (17)	46 (86)

the decrease in the percentage of negative calcium balances shown in Table II would seem to be of more definite significance. A corresponding comparison of the phosphorus balance figures, in relation to phosphorus intake, is given in Table V.

TABLE V.

Correlation between Phosphorus Intake Levels and Phosphorus Balances.
(Analysis of Group IV Cases—Calciferol only).

Intake per 48 hours	No. of balances	Balance positive	Equilibrium	Balance negative	Percentage negative balances
Below 2 g.	1 (2)	1 (1)	0 (1)	0 (0)	0 (0)
Between 2.1–2.5 g.	3 (13)	1 (1)	1 (1)	1 (11)	33 (84)
Between 2.6–3.0 g.	16 (11)	5 (4)	2 (4)	9 (3)	56 (36)
Between 3.1–3.5 g.	19 (15)	7 (11)	5 (0)	7 (4)	37 (27)
Between 3.6–4.0 g.	15 (17)	6 (7)	4 (2)	5 (8)	33 (46)
Between 4.1–4.5 g.	5 (12)	4 (7)	0 (2)	1 (3)	20 (40)
Between 4.6–5.0 g.	3 (5)	1 (3)	1 (0)	1 (2)	33 (40)
Over 5 g.	1 (4)	0 (3)	0 (1)	1 (0)	100 (0)

These figures are more difficult to interpret, though it would seem (after eliminating the extreme upper and lower limits of intake, covering a number of balances so small as to be statistically negligible) that a 48-hour intake of not less than 3 g. of phosphorus represents the minimum safety level.

OPTIMUM CALCIFEROL DOSAGE.

As was pointed out in a previous paper (Obermer, 1946b) dealing with the Calciferol factor, the women in Group III (calcium phosphate plus Calciferol) were given much larger doses than is usual in clinical practice. They were given 18,000 units up to the end of the fifth month, 27,000 during sixth and seventh months and then 36,000—the same dosage as cases 51 to 53 in the present paper. Although the results were significant, as is shown by the figures given in Table II, it was considered possible that smaller doses—in conjunction with calcium phosphate supplements—would have given just as good results. In planning the ascending scale of dosage in these Group IV cases, therefore, it was hoped that the results might point to an optimal zone of dosage.

A closer analysis of the figures in Section 2 of Table I, with this end in view, did not yield conclusive results. A comparison was made between the ratio of P in urine/P in faeces, calculated on the phosphorus intake and output figures, parallel to the calcium figures given in Sections 1 and 2 of Table I. It was difficult, if not impossible, to attach any importance to variations in this ratio. It is possible that the full figures for this ratio, covering the balances in the whole series of cases, and which will be given in the final report, may show some significant alteration in this ratio in Group III and Group IV cases as opposed to those who were not given Calciferol. Theoretically some such change should be found, if the action of Calciferol on human beings is at all similar to the action which has been experimentally observed in dogs (Shimotori and Morgan, 1943). However, from the series of balances determined on the cases discussed in this paper—admittedly too limited in number—we are not entitled to draw any dogmatic conclusions either as to the optimum dosage of Calciferol or as to the mechanism of Calciferol action. Taking the Group III and Group IV cases together, however, it is possible to make a provisional deduction:

That a dosage of less than 9,000 units in the first half of pregnancy and 18,000 units in the latter half does not show any definite evidence of an effective influence on either the calcium or phosphorus balances.

Analysis of Cases 37 to 53.

The balance figures mentioned below will be found by referring to Section 1 of Table I for "control" investigations and to Section 2 of Table I for investigations carried out during periods when the cases were ingesting supplements of Calciferol.

Case 37. Age 25; primipara. Height, 160 cm.; weight, 51 kg. Investigated 4 times. There were 2 control balances—at the 18th and 30th weeks; and 2 Calciferol balances—at the 24th and 36th weeks. All show positive calcium balances, except on the last occasion, in spite of very low calcium intakes (average of less than 1.1 g. per 24 hours). This case had very small stools throughout. This apparently was her habit at all times and though some of the stools were hard and faceted she suffered no discomfort.

Temperament. Exceptionally cheerful and well balanced—no worries.

Influence of Calciferol. No evidence that the 800 units per day in the Government capsule had any effect whatsoever.

Case 38. Age 22; primipara. Height, 170 cm.; weight, 72 kg. Investigated 3 times. No control balance as she took a Government capsule per day throughout pregnancy. One positive balance and 2 equilibria, in spite of a calcium intake which averaged 1.2 g. per day.

Temperament. Stupid and placid.

Influence of Calciferol. No definite evidence.

Case 39. Age 23; primipara. Height, 155 cm.; weight, 64.5 kg. Investigated 4 times. First control balance at 24th week; extremely low calcium intake. Heavy negative balance. The same applies to the first Calciferol balance (1,000 units per day) at the 31st week. Shortly after this investigation, during a routine examination at the antenatal clinic, her arterial pressure was found to be higher than was considered normal and she was put to bed. She had no abnormal symptoms and felt perfectly well, but as the pressure did not fall she was taken into the lying-in hospital at Brocket Hall at about the 36th week of her pregnancy. There she was dieted as well as rested. The "control" figures for the 38th week were collected when she was in bed there, though back on normal diet. She had not been taking her Calciferol supplement while in hospital. A negative balance will be noted. She was then put back on a daily dose of 2,000 units for the 15 days prior to the last Calciferol balance at the 40th week. On a calcium intake, which was practically identical to the intake at the 38th week, the balance had become positive.

Temperament. Cheerful and equable.

Influence of Calciferol. It is possible that as little as 2,000 units per day did, in fact, have a definite effect, in view of her temperament and the conditions of complete tranquility—she was a little bored but quite happy and cheerful.

CASE 40. Age 30; primipara. Height, 174 cm.; Weight, 77 kg. Investigated 4 times. The control balance at the 14th week was positive, though the phosphorus balance was negative. At the 20th week (1,000 units) and at the 26th and 31st weeks (2,000 units) the balances were negative.

Temperament. Over-conscientious—did far too much—no tranquility of mind.

Influence of Calciferol. No evidence.

CASE 41. Age 27, second pregnancy. Height, 171 cm.; weight, 60.5 kg. (Previous normal pregnancy and labour in 1944.) Investigated 4 times. Heavy negative control balance and negative balances at 15th week (1,000 units) and 27th week (2,000 units), equilibrium at the 21st week (1,000 units).

Temperament. Dissatisfied, always whining, incompetent, worried about trifles.

Influence of Calciferol. No evidence.

CASE 42. Age 23; primiparae. Height, 159 cm.; weight, 53 kg. Investigated 4 times. Exceptionally small control intake at 12th week (less than 0.6 g. per day). Heavy negative balance. At 18th week (3,000 units) positive balance, at 24th week (3,000 units) and 31st week (6,000 units) equilibria in spite of a consistently inadequate intake. The stools in this case were definitely " constipated " though no discomfort was experienced.

Temperament. Lethargic—never seemed to read or take an intelligent interest in anything—sat about ruminating.

Influence of Calciferol. It is probable that the relatively small doses of 3,000 and 6,000 units respectively did exert some influence in this case. It is difficult to avoid postulating that a given dosage of Calciferol exerts an influence in direct inverse proportion to the nervous excitability of the subject.

CASE 43. Age 33; second pregnancy. Height, 167 cm.; weight, 74.5 kg. (Previous pregnancy in 1944. Toxaemia, labour in April, 1944; 6 weeks premature, baby only lived 27 hours and died of convulsions.) Investigated 5 times. Control balance at 9th week—negative. At 15th and 21st weeks (3,000 units) negative balances. Equilibrium at 28th week and negative at 34th week (6,000 units on both occasions).

Temperament. Active, cheerful and well-balanced, but frightened of recurrence of foetal death and somewhat worried about inability to find flat for herself and husband—living with parents.

Influence of Calciferol. The initial increase of dosage from 3,000 to 6,000 may have had some effect. As her temperament was favourable and her conditions unfavourable a somewhat larger dose, together with a calcium phosphate supplement, might have been effective.

CASE 44. Age 32; primipara. Height, 159 cm.; weight, 62 kg. Investigated 4 times. (Figures for the first 3 occasions only shown on Table I.) Control balance heavily negative. Balance at 21st week (3,000 units) also negative. Balance at 28th week (6,000 units), positive. This case was again investigated at the 34th week. The figures have not been included, as she had been given a supplement of calcium phosphate by a new doctor at the antenatal clinic. The figures on this 4th occasion show a negative balance of 0.5 g. calcium, in spite of a calcium intake of 4.57 g. and a Calciferol dosage of 9,000 units.

Temperament. "Always been very highly strung, doctor" ; "nervous breakdown", February 1945 Fussed and worried throughout her pregnancy.

Influence of Calciferol. Doubtful.

CASE 45. Age 28; primipara. Height, 172 cm.; weight, 57 kg. Investigated 5 times. All balances heavily negative, in spite of a dosage of 3,000 units at the 15th week, 6,000 units at the 22nd and 28th weeks and 9,000 units at the 34th week.

Temperament. Pleasant woman but general physical condition poor—housing conditions very bad—generally harried—much worried about husband.

Influence of Calciferol. No evidence.

CASE 46. Age 25, primipara. Height, 155 cm.; weight, 54 kg. Investigated 5 times. No control balance as she was taking a Government capsule throughout her pregnancy, as well as the Calciferol supplement. At the 11th week (800 units)

balance was positive, probably because she passed unusually small stools. The balance at the 17th and 23rd weeks (3,800 units), the 29th week (8,800 units) and the 34th week (9,800 units) were all negative.

Temperament. " Highly strung "—very upset by bombing; bad housing conditions; unhappy and dissatisfied.

Influence of Calciferol. No evidence.

CASE 47. Age 27; primipara. Height, 162 cm.; weight, 49.5 kg. Investigated 5 times. Control balance negative. Equilibrium at the 21st week (9,800 units). Negative balance at the 27th week (9,800 units), positive balance at the 33rd week (9,800 units) and equilibrium at the 38th week (18,800 units).

Temperament. Equable; cheerful; exceptionally good sense of humour. This patient was subjected to both flying bombs and rockets during the first two-thirds of her pregnancy but they did not seem to worry her.

Influence of Calciferol. It is probable that the larger doses had a definite effect.

CASE 48. Age 26, primipara. Height, 158 cm.; weight 63.5 kg. Investigated 6 times. No control balance as she was taking a Government capsule as well as the Calciferol supplement throughout pregnancy. Equilibrium at 8th week (8,000 units). Negative balance at 14th and 20th weeks (9,800 units), positive balances at 26th (9,800 units) and 32nd week (18,800 units), equilibrium at the 38th week (27,800 units).

Temperament. Florid; cheerful; energetic; always optimistic, never worried.

Influence of Calciferol. It is probable that the higher dosage (18,000 units and over) had a definite effect. It should be noted that the calcium intake figures for this case were higher than the average in this series (up to 1.79 g. per day).

CASE 49. Age 31, primipara. Height, 162 cm.; weight 62 kg. Investigated 5 times. Control balance heavily negative. Balance at 16th week (9,000 units) equilibrium and slightly negative at the 24th and 30th weeks (18,000 units) and 36th week (27,000 units).

Temperament. " Worried ". Mother had nearly died of severe nephritis in pregnancy. She was frightened that she would follow suit.

Influence of Calciferol. As the calcium intake figures were consistently below 1.0 g. per day it is probable that the Calciferol exerted a definite influence.

CASE 50. Age 22, primipara. Height, 172 cm.; weight 63 kg. Investigated 4 times. Control balance slightly negative. At 27th week (18,000 units) balance positive, at 33rd week (27,000 units) equilibrium, and negative balance at 39th week (27,000 units). On this last occasion it should be noted that the calcium intake was only 0.78 g. per day.

Temperament. Cheerful, intelligent and well balanced.

Influence of Calciferol. Highly probable. If her calcium intake had been doubled throughout, her balance figures might well have been optimal.

CASE 51. Age 32, primipara. Height, 158 cm.; weight 65.5 kg.

CASE 52. Age 23, primipara. Height 177 cm.; weight, 74 kg.

CASE 53. Age 33, primipara. Height, 168 cm.; weight 54 kg.

These 3 cases can be discussed together as their Calciferol dosage was identical. The predominance of positive balances in Case 51 contrasts strongly with the predominantly negative balances in Case 52, and still more with the persistently heavy negative balances of Case 53.

CASE 51. The perfect example of a human ruminant. Few, if any, interests outside food and bed. It will be noted that her balance figures progressively improved, on increasing dosage, up to the last investigation at the 38th week, when she had an exceptionally large stool and an inadequate intake.

CASE 52. An intelligent and well-balanced woman who was very worried throughout her pregnancy by the necessity for finding a house or flat near her husband's work.

CASE 53. An extremely unfortunate temperament. The sort of woman who always considered

herself the victim of a specially malign fate. When she became pregnant she hesitated a long time before deciding to continue with it—was not in love with her husband and, throughout pregnancy, tortured herself with doubts as to the advisability of having a child and the consequences that would ensue.

Control balance at the 8th week was not representative, as only one small stool was passed and the figures had to be multiplied by 2 to arrive at an approximate balance. All the other investigations show a markedly negative balance.

Influence of Calciferol. As the calcium intake in these 3 cases was, roughly, similar (all below our " safety " level) and the diets of all 3 women more varied and abundant than the average for this series, it may be legitimate to assume that the dosage of Calciferol was adequate in Case 51—optimum temperament, tranquil life during pregnancy; less adequate in Case 52—favourable temperament, absence of tranquility during pregnancy; and totally inadequate in Case 53—unfavourable temperament, worry and anxiety during pregnancy.

The Temperamental and Emotional Factors.

All general practitioners with an extensive obstetric practice and practising obstetricians know that these factors are of great importance. It would be of great value, however, to be able to prove this fact in a quantitatively experimental manner. Unfortunately, however, it is extraordinarily difficult to bring forward statistical proof. On the other hand it is difficult to find any other explanation for (*a*) the significant proportion of negative balances found, in the cases of this series, who were given both adequate supplements of calcium phosphate and very high doses of Calciferol, that is, 22.5 per cent negative balances shown on Table II for Group III, and (*b*) the variable reaction of different Group IV cases to identical doses of Calciferol.

The Temperamental Factor.

It is logical to assume that the differences in endocrine tempo and autonomic balance, which underly temperament, influence the metabolic rhythm as a whole. Of recent years much work has been done on the influence of hormones and functional endocrine variations on metabolism. The reader is referred to Holmes (1945) for a general survey. A few references to the influence of the parathyroid (Albright, *et al.*, 1929; Ellsworth, 1932; Cantarow, Brundage and Housel, 1937), the pituitary (Bauer and Aub, 1941; Pugsley and Anderson, 1934; Schriver and Bryan, 1935), the thyroid (Althausen, Kerr and Stockholm, 1939; 1941; Johnston, 1941a), and the ovaries (Johnston, 1941b; Albright, Smith and Richardson, 1941) will be sufficient to give the reader a bird's-eye view of the work on this fascinating and complex subject. Further, the metabolic studies which have been carried out on all the cases in this series, and which will be published later, show that the degree of metabolic fluctuation is at least equal to one's clinical appreciation of temperamental variations.

The Emotional Factor.

It is a commonplace that anxiety and worry exert a profound influence on metabolism. The interpretation of the figures and statistics, which have been given in this paper, must needs be influenced by this factor. Anxiety has already been stressed by other workers in pre-war days (Macy, *et al.*, 1930). The degree of anxiety to which persistent bombing gave rise, in the cases of this series, from the beginning of the experiment in 1943 up to the end of the war in Europe in May 1945, can hardly be overestimated. It is known that the female pregnant organism is more labile than the non-pregnant one. A quantitative reflection of the effect of this factor is shown by

the fact that over 80 per cent of the urines passed by the cases investigated during the bombing periods contained quantities of glucose sufficiently large to be susceptible of measurement by delicate methods, in many cases much larger quantities. Very few urines passed by the cases investigated since May 1945 have contained appreciable quantities of a reducing substance. When considering the figures in Tables II, III, IV and V it should be remembered that Group IV cases—Cases 37 to 53—considered in this paper were, with one exception, investigated in the post-war period. It may well be, therefore, that the decreased number of negative balances in Group IV could partly, or even wholly, be accounted for by less anxiety, and might be only partly or, perhaps not at all, attributable to Calciferol.

This is only another example of the complexity of the subject of mineral metabolism. So many intrinsic and extrinsic factors are to be considered in each case that rash interpretations and generalizations needs must be invidious.

What is the Clinical Significance of Negative Calcium Balances?

To some, the fact that 80 per cent of the cases in this series who had no calcium or Calciferol supplements (controls—Table II) showed a negative calcium balance will seem a startling finding. On the other hand these cases are drawn from the labouring and middle classes—the overwhelming majority of the population. The author's experience, based on the metabolic investigation of some hundreds of pregnant women throughout pregnancy during the last 20 years, leads him to believe that these figures are representative. Can such a common phenomenon be considered pathological? On the one hand we have learnt to believe in the extraordinary powers of adaptation of the human organism to adverse circumstances. On the other hand we know that the foetal requirements for calcium during pregnancy (Mitchell and Curzon, 1939), exclusive of that of the maternal organism, are roughly 25, 50, 84, 125, 175, 234, and 300 mg. daily, respectively, for the last 7 lunar months. In theory, therefore, these persistently negative balances must result in some damage to the maternal organism and, in some cases, even to that of the foetus. It is to be hoped that the labour details as well as the maternal and foetal postnatal reports on the cases in this series, which will be published later, may throw some light on this important subject. It is imperative, also, that further studies of this nature and in larger numbers be carried out on normal pregnant women. These studies must be even more comprehensive and include a reliable method for assessing appreciable degrees of decalcification of the maternal skeleton, such as that of Mack *et al.* (1931). A statistically significant number of cases should, also, be included on adequate calcium phosphate supplements and given ascending doses of Calciferol. It should thus be possible to establish an optimum Calciferol dosage or, rather, a "safety" level for different temperaments and conditions of pregnancy. The findings of such a series would either bear out or contradict, with authority, the tentative conclusions to which the writer has been led by the figures derived from this preliminary experiment.

Practical Conclusions.

On the basis of the figures given in this and the two previous papers, which cover 227 forty-eight hour investigations, at different phases of pregnancy, the following tentative conclusions have been arrived at:

(1) That the phosphorus intake of

normal pregnant women on a generous all-round diet is usually adequate. When the diet is insufficient owing to poverty or any other reason, and we suspect that the daily intake of P is less than 1.5 g. per day, a supplement of phosphorus should be given.

(2) That the minimum "safety" levels of daily calcium intake are 2 g. of Ca element from the beginning of pregnancy to the end of the 7th month and 2.5 g. from the 8th month to term. These amounts cannot be arrived at without a supplement, however generous and all-round the diet. A pregnant woman who consumes her statutory pint of milk per day (0.72 g. Ca.) together with her daily ration of cheese (0.08 g. Ca) and a high average of "other foods" intake (0.30 g. Ca) arrives at a total 24-hour intake of only 1.1 g. To ensure adequate reserves every pregnant woman should be given a supplement of calcium phosphate, containing at least the following amounts of calcium and phosphorus elements:

	Ca	P
3rd to 5th months	0.64 g.	0.282 g.
6th to 8th months	0.95 g.	0.423 g.
8th month to term	1.26 g.	0.564 g.

(3) In the climatic conditions of Great Britain every pregnant woman also requires a supplement of Calciferol. The dosage should be varied according to her temperament and the emotional stresses and strains to which she is subjected during her pregnancy. 6,000 units during the first 6 months and 12,000 units during the last 3 months may be adequate for an exceptionally placid woman in conditions of tranquility. The dose for the average woman in average conditions should probably be not less than 10,000 units in the first 6 months and 20,000 during the last 3 months. Even these doses should be increased under favourable circumstances, playing on an unfavourable temperament.

(4) Small stools are desirable and even "constipation" should be tolerated, if it gives rise to no discomfort or mechanical trauma.

(5) Laxatives and drastic purgatives should be abstained from. Under exceptional circumstances small doses of paraffin or an agar preparation should be resorted to.

References.

Albright, F., Bauer, W., Ropes, M., and Aub, J. B. (1929): *J. clin. Invest.*, **7**, 139.

Albright, F., Smith, P. H., and Richardson, A. M. (1941): *J. Amer. med. Ass.*, **116**, 2465.

Althausen, T. L., Kerr, W. J., and Stockholm, M. (1939): *J. clin. Invest.*, **18**, 763.

Althausen, T. L., Kerr, W. J., and Stockholm, M. (1941): *J. clin. Invest.*, **20**, 438.

Bauer, W., and Aub, J. C. (1941): *J. clin. Invest.*, **20**, 295.

Cantarow, A., Brundage, J. T., and Housel, E. L. (1937): *Endocrinology*, **21**, 368.

Elsworth, R. (1932): *J. clin. Invest.*, **11**, 1011.

Holmes, J. O. (1945): *In* Wohl, G. W. (Ed.) *Dietotherapy*. Philadelphia, p. 180.

Johnston, J. A. (1941a): *Amer. J. Dis. Child.*, **62**, 1172.

Johnston, J. A. (1941b): *Amer. J. Dis. Child.*, **62**, 708.

Mack, P. B., O'Brien, A. T., Smith, J. M., and Bauman, A. W. (1931): *Science*, **89**, 467.

Macy, I. G., Hunscher, H. A., Nims, B., and McCosh, O. I. (1930): *J. biol. Chem.*, **86**, 17.

Mitchell, H. H., and Curzon, E. (1939): *The dietary requirement of calcium and its significance.* Actualities scientifiques et industrielles, No. 771. *Nutrition*, xviii. Paris, p. 101.

Obermer, E. (1946a): *J. Obstet. Gynaec.*, **53**, 269.

Obermer, E. (1946b): *J. Obstet. Gynaec.*, **53**, 362.

Pugsley, L. J., and Anderson, E. M. (1934): *Amer. J. Physiol.*, **109**, 85.

Schriver, W. deM., and Bryan, A. H. (1935): *J. clin. Invest.*, **14**, 212.

Shimotori, N., and Morgan, A. F. (1943): *J. biol. Chem.*, **147**, 201.

Studies in Prematurity, Stillbirth and Neonatal Death

Part II. Delivery and its Hazards.

BY

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Introduction.

In this series of studies a statistical analysis has been made of 7,599 births occurring in the Simpson Memorial Pavilion, Edinburgh during the 3-year period, 1942, to 1945 inclusive, in order to evaluate the principal aetiological factors influencing the incidence of prematurity, infant death and stillbirth.

As was pointed out in Part I (Drillien, 1947), a large number of similar surveys, with widely divergent conclusions, have been carried out during the past 15 years in America and elsewhere, and it was suggested that the main reasons for these discrepancies consist of the absence of adequate controls, failure to differentiate between emergency and booked cases, frequent omission of stillbirths when considering infant wastage, and the adoption of varying criteria of prematurity and viability. In the analysis of this series, a special code card was designed, on which were entered details from the infant and obstetric records of every premature birth, stillbirth and infant death occurring during the period, with a 1 in 10 sample, to act as a control group, of mature infants born in hospital and surviving their discharge.

The previous paper dealt with prematurity-rates and showed how closely outcome—whether the infant was stillborn, died or survived—was related to birthweight. The factors affecting birth-weight were then considered under 4 headings, complications of pregnancy, age of mother, legitimacy and sex of infant. This present paper deals with delivery and its hazards and Part III with deaths and stillbirths.

Modes of Delivery in Primiparae and Multiparae.

In Table I the distribution of modes of delivery is compared for booked and unbooked cases both for multiparae and primiparae, multiple births being excluded. The rates for the booked primiparae give the nearest approach to what would be expected in a random sample of first births in the general population. Comparing the rates for primiparae and multiparae the most striking feature is seen to be the excess of instrumental delivery among the former. In both booked and unbooked groups the rate is over 3 times that of the multiparae. In Table II the mode of delivery is compared in booked cases for premature and mature infants. Instrumental delivery is seen to be the more common for mature infants, and Caesarean section for the premature group.

Outcome According to Mode of Delivery.

Table III gives the outcome in the different modes of delivery for booked cases,

excluding multiple births. Unbooked cases have not been included, as their outcome is so largely determined by the complications of pregnancy for which the majority of emergency cases are admitted. There is a very great excess of deaths and stillbirths in breech deliveries and Caesarean section, and a smaller excess of stillbirths in cases of instrumental delivery. Table IV shows the wastage rates for different modes of delivery according to whether the infant was premature or mature. In each group the difference is also shown between wastage

3. There is an increased risk in Caesarean section for both premature and mature infants, especially the latter.

The excess wastage in breech delivery and Caesarean section may be due to:

1. Dangers inherent in the method of delivery itself.

2. Complications incident to or accompanying the method of delivery. The information relating to these 2 methods of delivery were therefore further investigated with special reference to these possible alternatives.

TABLE I.

Mode of Delivery, Excluding Multiple Births.

Mode of delivery	Primiparae		Multiparae	
	Booked per cent	Unbooked per cent	Booked per cent	Unbooked per cent
1. Vertex, spontaneous	80.4	48.5	87.1	69.4
2. Vertex, low forceps	8.0	8.1	1.3	1.5
3. Vertex, mid or high forceps	2.3	14.1	1.9	2.9
4. Version and extraction	5.5	6.1	1.3	4.8
5. Breech, assisted or spontaneous ...	2.2	6.5	2.9	10.8
6. Caesarean section	1.4	14.8	5.3	8.2
7. Craniotomy and other mutilating operations	0.1	1.8	0.1	2.3
Total	100.0	100.0	100.0	100.0
Number of cases	4249	446	1647	729

by each mode of delivery and that observed in cases of spontaneous vertex delivery. The rate for version and extraction is based on only 3 cases, and reliance cannot be placed upon it. The table suggests the following conclusions:

1. Instrumental delivery appears to be as safe as spontaneous vertex for premature infants though it carries an increased risk in the mature.

2. Breech delivery has a considerably greater wastage-rate than any other method in both premature and mature births.

Breech Delivery.

Breech delivery is commonly considered to be favoured by anything which prevents the head from engaging in the pelvic brim, such as placenta praevia or hydramnios. The dangerous complication of prolapse of the cord also occurs with increased frequency in breech presentation. These complications all carry a heavy mortality-rate. Table V gives the survival-rates in all breech deliveries, excluding cases of hydramnios, placenta praevia and prolapsed cord, and in spontaneous vertex deliveries excluding the same 3 complica-

TABLE II.

Mode of Delivery in Booked Cases, Excluding Multiple Births

Mode of delivery	Primiparae		Multiparae	
	Premature per cent	Mature per cent	Premature per cent	Mature per cent
1. Vertex, spontaneous	80.3	80.5	76.4	88.1
2. Vertex, low forceps	2.8	8.3	1.4	1.3
3. Vertex, mid or high forceps	0.8	2.4	0.7	2.1
4. Version and extraction	1.6	5.8	0.0	1.4
5. Breech, assisted or spontaneous ...	8.7	1.8	10.0	2.3
6. Caesarean section	5.5	1.2	11.4	4.7
7. Craniotomy and other mutilating operations	0.4	0.1	0.0	0.1
Total	100.0	100.0	100.0	100.0

TABLE III.

Outcome by Mode of Delivery in Booked Cases, Single Births

Mode of delivery	Primiparae			Multiparae		
	Per cent lived	Per cent died	Per cent stillborn	Per cent lived	Per cent died	Per cent stillborn
Vertex, spontaneous	96.9	1.2	2.0	95.1	1.7	3.2
Vertex, low forceps	96.2	1.5	2.4	95.4	0.0	4.5
Vertex, mid or high forceps	93.8	1.0	5.2	93.8	3.1	3.1
Version and contraction	95.3	0.9	3.8	95.2	0.0	4.8
Breech	75.5	10.6	13.8	74.9	10.4	14.6
Caesarean section	81.7	10.0	8.3	91.9	5.7	2.3
Craniotomy, etc.			100.0			100.0

TABLE IV.

Percentage Wastage (Dead + Stillborn) by Mode of Delivery, Compared with Spontaneous Vertex, All Booked Single Births.

Mode of delivery	Premature		Mature	
	Wastage per cent	Difference from spontaneous vertex	Wastage per cent	Difference from spontaneous vertex
Vertex, spontaneous	33.8	—	1.6	—
Vertex, all forceps	33.3	− 0.5	3.8	+ 2.1
Version and extraction	25.0	− 8.8	4.4	+ 2.8
Breech	52.8	+19.0	15.1	+13.5
Caesarean section	36.7	+ 2.9	6.0	+ 4.4

tions. Even when the dangerous complications commonly occurring with breech delivery are excluded, there still seems to be a definite risk to the foetus, which is greater for mature than for premature infants. Here the survival-rate is 17.6 per cent less than in spontaneous vertex delivery, a difference which is statistically highly significant. The next paper in this series will show the importance of asphyxia and intracranial haemorrhage in deaths and stillbirths occurring with breech delivery.

TABLE V.

Comparison of Survival Rates in Spontaneous Vertex and Breech Deliveries. All Single Births.

	Per cent survivors	Difference from spontaneous vertex	Standard deviation of difference	t
Premature:				
Vertex, spontaneous	61.5			
Breech (all)	39.2	−22.3	6.53	3.4
Breech (excluding complications)	48.0	−13.5	7.77	1.7
Mature:				
Vertex, spontaneous	100.0			
Breech (all)	79.5	−20.5	4.36	4.7
Breech (excluding complications)	82.4	−17.6	3.87	4.5

TABLE VI.

Indications for Caesarean Section. All Single Births.

	Premature	Mature	Total
1. Contracted pelvis, elective	4	84	88
2. Contracted pelvis, emergency	0	44	44
3. Local disease, elective	4	11	15
4. Chronic maternal disease, elective	5	10	15
5. Severe toxaemia, emergency	27	40	67
6. Placenta praevia, emergency	17	15	32
7. Following ruptured uterus, emergency... ...	0	2	2
8. Others, emergency	0	10	10
Total	57	216	273

Caesarean Section.

Cases delivered by Caesarean section fall into the following categories:

1. Contracted pelvis. Either controlled trial labour or elective Caesarean section.

2. Emergency cases of contracted pelvis, admitted after prolonged labour, or with uterine inertia, or following failed forceps outside.

3. Local disease of uterus, such as fibroids, or of ovaries, such as cysts or other new growths. Elective Caesarean section.

4. Chronic maternal disease, such as cardiac disease, diabetes, chronic nephritis. Elective Caesarean section.

5. Severe toxaemias. Emergency cases, often admitted with some other complicating factor, chronic co-existent maternal

disease, bad obstetric history, or occurrence in an elderly primipara.

6. Placenta praevia, emergency cases.

7. Following ruptured uterus, emergency cases.

8. Other causes.

The numbers in each of these 8 categories are shown in Table VI. The next table gives the survival-rates for premature and mature infants in cases of elective Caesarean section (categories 1, 3, and 4), emergency Caesarean section (categories 2, 5, 6, 7, and 8), and a control group of spontaneous vertex delivery in booked cases only.

In the premature group an elective Caesarean section seems to be a rather safer method of delivery than a spontaneous vertex, but the difference, being less than its standard deviation, is quite insignificant. The only significant difference is in the mature group, where emergency Caesarean sections seem to carry a definite risk as compared with spontaneous vertex delivery.

TABLE VII.

Comparison of Survival Rates in Spontaneous Vertex and Caesarean Section Deliveries. All Single Births.

	Per cent survivors	Difference from spontaneous vertex	Standard deviation of difference	t
Premature:				
Vertex, spontaneous	66.2	—		
Caesarean section, elective	76.9	+10.7	12.04	0.89
Caesarean section, emergency	59.1	− 7.1	7.95	0.89
Mature:				
Vertex, spontaneous	98.4	—		
Caesarean section, elective	95.2	− 3.2	2.49	1.29
Caesarean section, emergency	90.1	− 8.3	3.91	2.12

TABLE VIII.

Mode of Delivery by Maternal Age: Primiparae Except Multiple Births.

Mode of delivery	Mothers 15 to 24 per cent	Mothers 25 to 34 per cent	Mothers 35 to 44 per cent
Vertex, spontaneous	81.5	75.1	50.2
Vertex, forceps (low, mid and high)	7.5	15.8	20.9
Version and extraction	5.2	5.1	13.6
Breech	3.5	1.6	1.3
Caesarean section	2.2	2.1	13.2
Craniotomy, etc.	0.2	0.4	0.8
Total	100.0	100.0	100.0

Comparison with Results of Other Workers.

In trying to compare these results with those in the literature, the same kind of difficulties were encountered as in the case of complications of pregnancy discussed in Part I. Here again the findings of different authors differed widely. In an analysis

of 17,728 deliveries at the Chicago Lying-in Hospital, Potter and Adair (1938) found the highest wastage-rate (deaths plus still-births) among infants delivered by version and extraction. The mortality was nearly twice as high as the next most dangerous group, breech delivery. Considering premature babies only, Dibble and Plass (1942) agree that version and extraction carries the greatest risk, though Clifford (1934a), also dealing with premature births, found the highest mortality occurred with breech delivery with Caesarean section a close second. Breese (1938) is of the opinion that the difference in mortality-rates between breech and vertex deliveries is accounted for by the fact that in the former case the babies were about 250 g. less in weight on the average, and that in Caesarean section there was no deleterious effect that could not be accounted for by birth-weight of the infant.

Mode of Delivery by Maternal Age.

Table VIII gives the distribution of modes of delivery of all primiparae, excluding multiple births, in 3 maternal age-groups, and the data are also shown in Fig. 1. The percentage of spontaneous vertex deliveries falls with increasing age, while the incidence of instrumental deliveries rises. Version and extraction, and Caesarean section rise sharply in the highest age group. Breech delivery is rather commoner in the youngest mothers. The figures for booked cases show the same general picture, though there is a slightly lower incidence of abnormal delivery in all age groups, and a correspondingly higher percentage of spontaneous vertex cases. The same information is shown in graphical form in Fig. 2 for premature and mature infants separately. Here spontaneous vertex deliveries are omitted and forceps and version and extraction are grouped together as "instrumental". The figure shows that the fall in the percentage of normal spontaneous deliveries with age is especially marked with mature infants, of whom less than half were so delivered in the oldest age group of mothers, amongst whom instrumental deliveries occurred in 39 per cent of the cases.

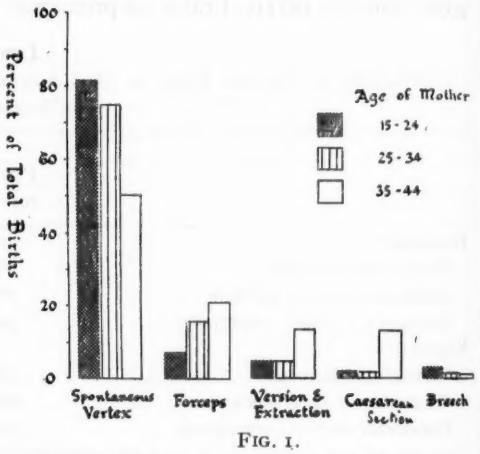

FIG. 1.

Mode of delivery in relation to age of mother.

Complications of Delivery.

The complications of delivery observed in this series of cases were as follows:

1. Prolapsed cord.

2. Malpresentation (e.g., brow, face, persistent occipito-posterior), including compound presentation.

3. Contracted pelvis.

4. Uterine inertia.

5. Deep transverse arrest.

6. Prolonged labour, not including cases already classified under 3, 4 and 5 above. Labour was taken to be abnormally prolonged when lasting more than 36 hours in primiparae and 24 hours in multiparae. It is realized that a better criterion would be the length of the second stage, but this information was frequently not available.

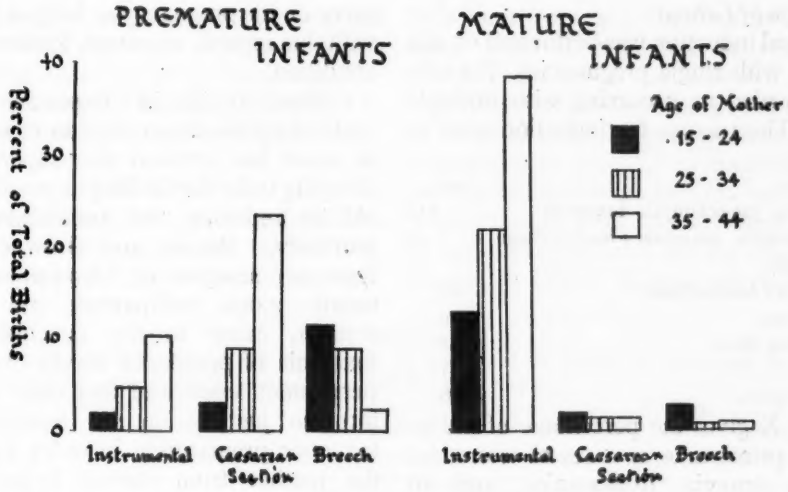

FIG. 2.
Mode of delivery in relation to age of mother and maturity of infant.

TABLE IX.
Incidence and Survival of Cases with Complications of Delivery: Booked Primiparae Except Multiple Births.

Complication of delivery	Number of cases	Premature incidence per cent	Mature incidence per cent	All babies incidence per cent	Survivors per cent
Prolapsed cord	19	1.1	0.4	0.4	36.1
Malpresentation	131	1.9	3.1	3.1	83.7
Contracted pelvis	58	1.1	1.4	1.4	88.1
Uterine inertia	45	0.4	1.1	1.0	90.0
Deep transverse arrest	108	0.8	2.6	2.5	92.3
Prolonged labour	144	3.8	3.3	3.3	87.9
Others	11	0.0	0.3	0.3	58.8
Total	516	9.1	12.2	12.0	

7. Others, including tonic uterine contractions, ruptured uterus, premature separation of placenta, and contraction ring.

Table IX shows the number and percentages of these complications occurring in booked primiparae, excluding multiple births, together with survival rates.

The complication of prolapsed cord is seen to carry a high mortality, only just over one third surviving. This may be due in part to the increased risk of other coexistent complications, such as placenta praevia, hydrammios, and congenital deformities, particularly anencephalus. The survival-rates for premature and mature infants was approximately the same, being 33.3 per cent and 37 per cent respectively.

Induction of Labour.

Surgical induction was performed on 264 patients with single pregnancies. No case was recorded as occurring with multiple births. The reasons for induction were as follows:

Toxaemias	146
including pre-eclamptic toxaemia	115
pre-eclamptic toxaemia + haemorrhage	10
eclampsia	16
Antepartum haemorrhage	62
Hydramnios	9
Intrauterine death	8
Nephritis	1
No cause given	38

Table X gives the percentage of inductions in primiparae in cases of toxaemia, placenta praevia, hydramnios, and all other cases. About one case in 11 of toxaemia had an induction, 1 in 7 of placenta praevia, 1 in 5 of hydramnios, and 1 in 250 of all other pregnancies. Table XI compares the percentage of infants under $3\frac{1}{2}$ pounds and $5\frac{1}{2}$ pounds in weight in induced pregnancies in primiparae, as compared with those allowed to go into labour without interference.

TABLE X.

Surgical Induction in Relation to Complications of Pregnancy: All Primiparae Except Multiple Births.

	Number of cases	Number of surgical inductions	Per cent surgical inductions
Toxaemia	718	64	8.9
Placenta praevia	65	9	13.8
Hydramnios	26	5	19.2
All other cases of pregnancy	3883	17	0.4

It has been shown in the previous paper (Part I) that an infant's chance of survival depends largely on its weight at birth, and also that toxaemia in the mother does not appear to have any adverse effect on the foetus apart from the effect on weight, as far as can be judged from survival-rates. It is therefore of the utmost importance to carry on the pregnancy as long as possible, with due regard, of course, to the mother's condition.

Clifford (1934b), in a paper describing a method for the determination of foetal size *in utero* has stressed the importance of delaying induction as long as possible as an aid to reducing the premature infant mortality. Barnes and Browne (1945), from an analysis of blood-pressures of nearly 2,000 nulliparous and parous women, came to the conclusion that toxaemia of pregnancy leaves of itself no permanent lesion and that there is therefore no justification for terminating a toxaemic prematurely in order to protect the mother from chronic hypertension. They point out, however, that the pregnancy may have to be interrupted if there seems to be a risk of eclampsia, or in the case of severe toxaemia to prevent death *in utero*. With regard to this last condition, there does seem to be a definite risk of a macerated foetus being associated with toxaemia, and this will be discussed more fully in Part III.

Table XI shows that surgical induction for toxaemia of pregnancy resulted in 8.3 per cent of the infants being less than $3\frac{1}{2}$ pounds and 37.7 per cent less than $5\frac{1}{2}$ pounds, these rates being more than $2\frac{1}{2}$ times as high as in cases of toxaemia allowed to go into spontaneous labour; though of course it must be remembered

that the more serious cases will be selected for induction, and even if they were left alone these cases would be more likely to go into premature labour than those in which the toxaemia was less severe.

SUMMARY.

This paper comprises the second study in a series based on nearly 8,000 births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive. In this part are considered different modes of delivery and their special hazards.

A large excess of instrumental deliveries was found in first births. There was a marked excess of stillbirths and deaths in breech delivery and Caesarean section, and a smaller excess, of stillbirths only, in instrumental deliveries. For premature infants instrumental delivery appeared to carry no extra risk, but breech delivery was very dangerous.

Incidence of spontaneous vertex delivery falls markedly with increasing maternal age, while instrumental deliveries and Caesarean section rise. Breech delivery is slightly more common in young mothers.

Surgical induction was performed most commonly in cases of hydramnios, antepartum haemorrhage and toxaemia. The proportion of very small babies in cases of induction was much greater than in cases going into labour without interference.

TABLE XI.

Percentages of Infants of Low Birth Weights in Induced and Non-induced Cases with Complications of pregnancy: All Primiparae Except Multiple Births.

Complication of pregnancy	Infants below 3 pounds 9 ounces		Infants below 5 pounds 9 ounces	
	Per cent of all non-induced cases	Per cent of all induced cases	Per cent of all non-induced cases	Per cent of all induced cases
Pre-eclamptic toxaemia	3.2	7.0	14.4	32.2
Eclampsia	5.8	6.3	19.3	37.6
Pre-eclamptic toxaemia with haemorrhage	6.3	10.0	31.3	70.0
All toxaemias	3.0	8.2	14.2	37.7
Antepartum haemorrhage	17.6	6.4	47.4	22.5
Hydramnios	20.5	88.9	38.7	88.9

REFERENCES.

Barnes, J., and Browne, F. J. (1945): *J. Obstet. Gynaec.*, **52**, 1.

Breese, B. B. (1938): *J. Pediat.*, **12**, 648.

Clifford, S. H. (1934a): *J. Pediat.*, **5**, 139.

Clifford, S. H. (1934b): *J. Amer. med. Ass.*, **103**, 1117.

Dibble, A. W., and Plass, E. D. (1942): *Amer. J. Obstet. Gynec.*, **44**, 279.

Drillien, C. M. (1947): *J. Obstet. Gynaec.*, **54**, 300.

Potter, E. L., and Adair, F. L. (1938): *J. Amer. med. Ass.*, **112**, 1549.

Part III. Stillbirths and Neonatal Deaths.

Introduction.

This paper forms Part III of a series of statistical studies into the aetiology of prematurity, infant death and stillbirth, based on 7,599 births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive.

Data from infant and obstetric records of every stillbirth, neonatal death and premature birth occurring during the 3-year period were entered upon a specially designed code card, together with data of a 1-in-10 sample of mature surviving infants, to act as a control group. The 2 previous parts (Drillien, 1947a; 1947b) dealt with prognosis according to birthweight, the principal factors affecting weight, and the special hazards of different modes of delivery. This paper deals with deaths and stillbirths.

Deaths.

1. *Age at Death.*

The number of infant deaths recorded was 204, with the age distribution shown in Table I. There were 195 deaths within 28 days of birth; of the 9 that occurred after the first month 7 were premature babies, of whom 5 were below $3\frac{1}{2}$ pounds in weight, and 2 suffered from gross congenital deformity which was the cause of death. The table shows that over 40 per cent of the

Table I.

Age at Death, All Cases.

Age at death	Number of deaths	Per cent of deaths	Premature, per cent	Mature, per cent
0 to 6 hours	39	19.1	22.5	11.3
7 to 12 hours	20	9.8	13.4	1.6
13 to 24 hours	27	13.2	14.1	11.3
Total, 1st day	86	42.2	50.0	24.2
1st day	86	42.2	50.0	24.2
2nd day	34	16.7	14.1	22.6
3rd day	14	6.9	5.6	9.7
4th day	9	4.4	3.5	6.5
5th day	7	3.4	2.8	4.8
6th day	10	4.9	4.9	4.8
7th day	5	2.5	1.4	4.8
Total, 1st week	165	80.9	82.4	77.4
1st week	165	80.9	82.4	77.4
2nd week	12	5.9	4.2	9.7
3rd week	15	7.4	7.1	8.1
4th week	3	1.5	1.5	1.6
Total, 1st month ...	195	95.6	95.1	96.1
After 1st month	9	4.4	4.9	3.9
Total	204	100.0	100.0	100.0

deaths took place on the first day, of which nearly half were in the first 6 hours. It is hard to draw the line between these very early deaths and stillbirths, as the aetiological factors affecting both are very similar. This emphasizes the importance of considering stillbirths as well as deaths when discussing infant wastage. The table also shows the percentage distribution by age of death of premature and mature infants, and these data are plotted as cumulative percentages in Fig. 1. Nearly a quarter of all the premature deaths took

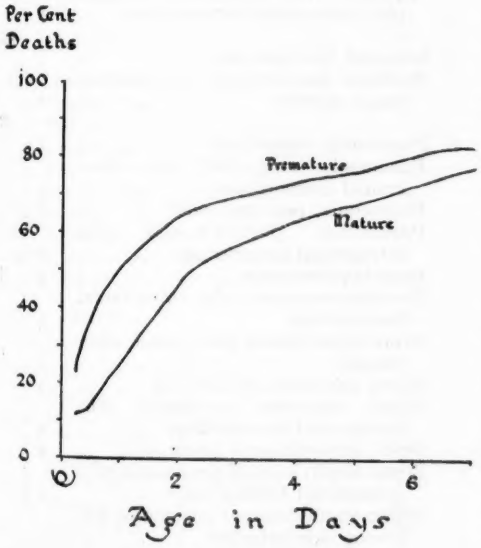

FIG. 1.
Cumulative curves of age at death.

place within 6 hours of birth, and one-half on the first day, these proportions being twice as high as those for mature infants. However good may be the care of premature babies, treatment after birth could have little effect in preventing these early deaths. Blackfan and Yaglou (1933) describe a routine of treatment for premature infants, but state that this was unable to influence the death-rate, 80 per cent of the total occurring during the first 48 hours. Clifford (1934) relates how deaths after the first 48 hours were reduced over a period of 6 years after the establishment of air-conditioned nurseries and other measures, but he also found that the rate for the first 48 hours was unaffected.

2. *Causes of Death.*

The diagnosis of the cause of death in 173 of the cases was based on autopsy findings. In the remaining 31 cases the diagnosis was made as follows: Obvious congenital defect, 16. Deaths in premature infants, no other clinical findings, 12. Asphyxia diagnosed clinically, 1. Intracranial haemorrhage, diagnosed by lumbar puncture, 1. Gastro-enteritis, diagnosed clinically, 1.

Causes of death have been divided into the following main categories:

1. Erythroblastosis foetalis.

2. Gross congenital defect. In a number of cases the immediate cause of death was infection, most commonly pneumonia.

3. Prematurity. This includes cases going to autopsy in which no pathological lesion could be detected apart from atelectasis, and in some cases a slight degree of subarachnoid and intraventricular haemorrhage. In a smaller number of cases autopsy was not performed, and no clinical diagnosis was made apart from prematurity.

4. Asphyxia. These cases showed subserous petechial haemorrhages, and often inhalation of liquor amnii and vernix, with or without commencing pneumonic changes. Intracranial haemorrhage was also found in a number of cases. Where subarachnoid or intraventricular haemorrhage occurred together with other signs of asphyxia, the haemorrhage was con-

sidered to be secondary to the asphyxia. In a smaller number of cases asphyxia was found together with a subdural haemorrhage. Here it is difficult to decide whether asphyxia or haemorrhage was the primary condition. These cases have been included under asphyxia.

5. Intracranial haemorrhage, subdural or intradural haemorrhage associated with birth trauma. In certain cases subdural haemorrhage occurred together with pneumonia. These cases have been included with pneumonia.

6. Pneumonia.

7. Meningitis.

8. Gastro-enteritis. Cases with a terminal pneumonia have been included in this group.

9. Congenital syphilis.

10. Others.

Table II gives causes of death in detail.

In Table III the causes of death are sub-classified by birth-weights. In the smallest infants prematurity alone accounts for nearly half the deaths, and with asphyxia and pneumonia included, for over 85 per cent of deaths. In the large premature babies, nearly one-third of the deaths are due to asphyxia and one-sixth to pneumonia, while congenital defects plus erythroblastosis account for a quarter of the deaths. In the mature group, congenital defects are by far the most important causes of death, accounting with erythroblastosis for about 55 per cent of fatalities. Section (*c*) of the table gives the death-rates per 1000 live births. This shows that in spite of the importance of congenital defects as a cause of death in mature infants their death-rate from this cause is a small fraction of that found among the premature. For all premature infants the death-rate from congenital defects is about 100 times that found for mature babies.

TABLE II.

Causes of Death.

1. Erythroblastosis		15	
Erythroblastosis plus meningitis		1	
			16
2. Congenital defects			41
3. Prematurity:			
No autopsy		12	
Autopsy, atelectasis only		12	
Autopsy, slight intracranial haemorrhage		15	
			39
4. Asphyxia		14	
Asphyxia plus sub-dural haemorrhage		6	
Asphyxia plus sub-arachnoid, intraventricular, or intracerebral haemorrhage		9	
Asphyxia plus pneumonic changes		11	
Asphyxia plus pneumonic changes plus intracranial haemorrhage		5	
			45
5. Subdural haemorrhage		7	
Subdural haemorrhage plus haemorrhagic disease		1	
			8
6. Pneumonia, unspecified		2	
Pneumonia, unspecified plus intracranial haemorrhage		3	
Pneumonia, post-asphyxial		4	
Pneumonia, post-asphyxial plus intracranial haemorrhage		2	
Bronchopneumonia		3	
Bronchopneumonia plus intracranial haemorrhage		4	
Bronchopneumonia plus thrush oesophagitis		1	
Septic inhalation pneumonia		3	
Septic inhalation pneumonia plus intracranial haemorrhage		3	
Septic staphylococcal pneumonia		4	
Septic staphylococcal pneumonia plus intracranial haemorrhage		2	
Septic staphylococcal pneumonia following skin infection		3	
			34
7. Meningitis, *B. coli*			2
8. Gastro-enteritis		9	
Gastro-enteritis plus pneumonia		2	
			11
9. Congenital syphilis			1
10. Other causes:			
Exsanguination		2	
Massive pulmonary haemorrhage		1	
Suprarenal haemorrhage		1	
Meconium peritonitis		1	
Gastric ulceration and haemorrhage		1	
Accidental asphyxia		1	
			7
Total			204

TABLE III.

Deaths by Birth-weights

(a) *Number of deaths*	Below 3 pounds 9 ounces	3 pounds 9 ounces to 5 pounds 8 ounces	5 pounds 9 ounces and over	All weights
1. Erythroblastosis	1	7	8	16
2. Congenital defects	5	10	26	41
3. Prematurity	33	6	0	39
4. Asphyxia	13	22	10	45
(4a. Asphyxia plus subdural haemorrhage)	(7)	(9)	(4)	(20)
5. Intracranial haemorrhage	0	4	4	8
6. Pneumonia	15	12	7	34
7. Meningitis	0	0	2	2
8. Gastro-enteritis	2	5	4	11
9. Congenital syphilis	0	1	0	1
10. Other causes	2	4	1	7
Total	71	71	62	204
(b) *Percentages*				
1. Erythroblastosis	1.4	9.9	12.9	7.8
2. Congenital defects	7.0	14.1	41.9	20.1
3. Prematurity	46.5	8.4	0.0	19.1
4. Asphyxia	18.3	31.0	16.1	22.1
5. Intracranial haemorrhage	0.0	5.6	6.5	3.9
6. Pneumonia	21.1	16.9	11.3	16.7
8. Gastro-enteritis	2.8	7.0	6.5	5.4
10. Other causes (including meningitis and congenital syphilis)	2.8	7.0	4.8	4.9
Total	100.0	100.0	100.0	100.0
(c) *Rates per 1,000 births.*				
1. Erythroblastosis	10	14	0.12	2.1
2. Congenital defects	51	19	0.39	5.4
3. Prematurity	333	12	0.00	5.1
4. Asphyxia	131	42	0.15	5.9
5. Intracranial haemorrhage	0	8	0.06	1.1
6. Pneumonia	152	23	0.11	4.5
8. Gastro-enteritis	20	10	0.06	1.5
10. Other causes (including meningitis and congenital syphilis)	20	10	0.05	1.3
Total	717	138	0.94	26.9

3. *Age at Death in Relation to cause of Death.*

Table IV shows that of all infants dying from prematurity or asphyxia, two-thirds died within the first 24 hours, and about 90 per cent within 3 days. Of those dying from congenital defects and erythroblastosis, 40 per cent lived longer than 3 days, and nearly 20 per cent survived for longer than 1 week. As would be expected, infections have a later age incidence. Nearly 40 per cent of all cases of pneumonia died after the first week, and all the fatal cases of gastro-enteritis survived their first week.

These figures further emphasize the comparatively minor role that treatment after

TABLE IV.

Age at Death by Cause of Death.

Cause of death	Percentage of deaths by the end of: 1st day	2nd day	3rd day	1st week
Congenital defects and erythroblastosis	36.8	50.8	57.8	82.4
Prematurity	66.7	79.5	89.7	97.4
Asphyxia	64.4	88.8	93.2	95.5
Intracranial haemorrhage	25.0	75.0	75.0	100.0
Pneumonia	8.8	26.4	38.2	61.8
Gastro-enteritis	0.0	0.0	0.0	0.0

birth plays in the reduction of neonatal mortality beyond the level at present attained under good hospital conditions. As has been previously shown, deaths in the first 48 hours are little affected by improvements in treatment, and deaths from gross congenital defect are also obviously not amenable to any measures taken postnatally. It would therefore appear that the most effective further improvement in postnatal treatment of the infant would be measures to prevent the later infections.

4. *Cause of Death in Relation to Complications of Pregnancy.*

Table V and Fig. 2 show the incidence of toxaemia, antepartum haemorrhage and other complications in the mother, for infants who died from certain specified conditions, in comparison with their incidence in mothers of babies who survived. The incidence of complications among mothers of babies with congenital defects is only slightly greater than among mothers of infants who survived. With every other cause of death the incidence of complications is much higher. Of babies dying from prematurity over 50 per cent of the mothers suffered from toxaemia or antepartum haemorrhage, and in the case of asphyxia the proportion was more than 70 per cent, antepartum haemorrhage being associated with 44 per cent of these deaths. By con-

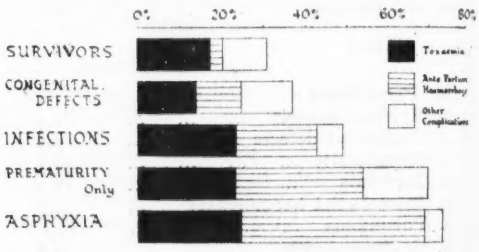

FIG. 2.
Cause of death in relation to maternal complications.

TABLE V.

Cause of Death by Complications of Pregnancy.

Cause of death	None per cent	Toxaemias, per cent	Antepartum haemorrhage, per cent	Others, per cent	Total, per cent
Congenital defects and erythroblastosis	63.1	14.0	10.5	12.3	100.0
Prematurity	30.8	23.1	30.8	15.4	100.0
Asphyxia	26.7	24.4	44.4	4.4	100.0
Intracranial haemorrhage	25.0	62.5	0.0	12.5	100.0
Infections	51.0	23.4	19.2	6.4	100.0
Other causes	37.5	12.5	25.0	25.0	100.0
Survivors	69.2	17.1	3.0	10.7	100.0

trast, the incidence of these complications in the mothers of survivors was 17 per cent of toxaemia, and 3 per cent of antepartum haemorrhage. The high toxaemia rate seen in cases of intracranial haemorrhage is associated with a greater frequency of forceps delivery in women with toxaemia. The percentage is based on only 6 cases.

5. *Cause of Death in Relation to mode of Delivery.*

Table VI compares the incidence of different modes of delivery in cases of death from certain specified causes with that obtained in infants who survived. The main points to be noted are:

TABLE VI.

Cause of Death by Mode of Delivery.

Cause of death	Spontaneous vertex, per cent	Instrumental, per cent	Breech, per cent	Caesarean section, per cent	Total, per cent
Congenital defects and erythroblastosis	66.7	5.3	19.2	8.8	100.0
Prematurity	59.0	0.0	23.1	17.9	100.0
Asphyxia	53.3	2.2	28.9	15.6	100.0
Intracranial haemorrhage	12.5	50.0	37.5	0.0	100.0
Infections	68.1	14.9	14.9	2.1	100.0
Other causes	62.5	0.0	12.5	25.0	100.0
Survivors	66.7	13.4	4.6	3.8	100.0

The high incidence of breech delivery in infants dying of congenital defects, prematurity, asphyxia and intracranial haemorrhage. In the first 2 conditions the mode of delivery is most likely a consequence of the abnormal foetus, whereas deaths due to asphyxia and intracranial haemorrhage were probably directly due to the breech delivery.

Intracranial Haemorrhage.

Table VII shows the total number of cases in which intracranial haemorrhage was found, irrespective of whether or not the haemorrhage was considered to be the cause of death, or whether the principal aetiological factor was adjudged to be asphyxia or birth trauma. Gross subdural haemorrhage due to birth injury is seen to occur with much the most frequency in mature deaths, though the contrast is not so marked with slight degrees of haemorrhage. On the other hand, subarachnoid, intraventricular and intracerebral haemorrhages, either alone or in combination, occur almost exclusively in premature infants. These latter forms of haemorrhage are most probably due to asphyxia, and occur more commonly in premature infants because of incomplete development of muscle and elastic tissue in the walls of the veins.

Section (*c*) of the table shows the incidence of different forms of haemorrhage per 1,000 live births according to mode of delivery. A high proportion of all types of intracranial haemorrhage was found in breech deliveries. This may be accounted for by the relatively large number of premature infants delivered by the breech, and to the special dangers in this mode of delivery of asphyxia, and of too rapid delivery of the head.

Pneumonia.

The diagnosis "pneumonia" in this classification covers a number of conditions:

TABLE VII.

Deaths from Intracranial Haemorrhage.

	Below 3 pounds 9 ounces	3 pounds 9 ounces to 5 pounds 8 ounces	Over 5 pounds 8 ounces	Total
(a) Numbers of cases.				
Subdural	1	4	8	13
Subdural (slight)	5	7	5	17
Subarachnoid	5	2	1	8
Intraventricular	10	4	0	14
Multiple (subarachnoid and/or intraventricular and/or intracerebral)	9	3	0	12
Intradural	0	0	1	1
Total	30	18	17	65
(b) Deaths as percentage of total weight in group.				
Subdural	1.4	5.6	12.9	
Subdural (slight)	7.0	7.0	11.3	
Subarachnoid	7.0	2.8	1.6	
Intraventricular	14.1 — 33.8	5.6 — 12.6	0.0 — 1.6	
Multiple	12.7	4.2	0.0	
Intradural	0.0	0.0	1.6	
	Spontaneous vertex	Instrumental	Breech	Caesarean
(c) Deaths per 1,000 live births by mode of delivery.				
Subdural	0.5	7.6	13.9	0.0
Subdural (slight)	1.5	3.2	17.4	3.8
Multiple	4.4	0.0	31.4	3.8
Total	6.4	10.8	62.7	7.6

1. Postasphyxial, occurring in a lung which is already atelectatic or filled with liquor amnii.

2. Bronchopneumonia, occurring either in the form commonly seen in elderly infants, or in a massive confluent form.

3. Septic staphylococcal pneumonia, with multiple suppurating foci, sometimes resulting from septic skin infections and septicaemia.

4. Septic inhalation pneumonia resulting from aspiration of milk or regurgitation of stomach contents.

5. Pneumonia not further specified.

6. Inhalation of excessive liquor amnii and vernix in an asphyxiated infant with commencing inflammatory changes. These cases died before gross pneumonic changes could occur.

Types 1 to 5 are listed under "pneumonia" in the previous classification, and type 6 under "asphyxia".

The numbers of the different types of pneumonia found in the 204 deaths were as follows:

Postasphyxial pneumonia	7
Bronchopneumonia	8
Septic staphylococcal pneumonia	8
Septic inhalation pneumonia	6
Unspecified pneumonia	6
Inhalation and inflammation	16
Total	51

Over 90 per cent of cases of inhalation with inflammatory changes and of post-

asphyxial pneumonia died within 48 hours of birth, whereas 86 per cent of the cases of septic staphylococcal, septic inhalation and bronchopneumonia died after the third day, and 55 per cent of them after the end of the first week.

TABLE VIII.
Deaths and Stillbirths from Congenital Defects by Maternal Age.

Age of mother	Primiparae Number of cases	Primiparae Rate per 1,000 births	Multiparae Number of cases	Multiparae Rate per 1,000 births
15 to 19	6	16.6	—	—
20 to 24	25	10.4	5	15.6
25 to 29	14	10.0	11	15.7
30 to 34	7	13.0	17	21.8
35 to 39	7	27.3	14	24.8
40 to 44	—	—	5	22.3

Congenital Defects and Age of Mother. Deaths and Stillbirths.

Table VIII shows the number of fatal congenital defects and the rate per 1,000 births according to maternal age. There appears to be a rise in the death-rate for mothers over 30 in both primiparae and multiparae. The rates for mothers under 30 and over, are as follows:

Primiparae:
Under 30. 10.8 per 1,000 births
30 and over 17.0 per 1,000 births

Multiparae:
Under 30 15.8 per 1,000 births
30 and over 22.9 per 1,000 births

On applying a combined probability test the 2 differences, considered together, are found to be just significant, in spite of the small number of cases. The rise with age of mother is in accord with the findings of Penrose (1946) that increasing maternal age is significantly related to the incidence of anencephaly, spina bifida and congenital hydrocephalus, and of Malpas (1937) who made a similar observation for congenital deformities as a whole.

STILLBIRTHS.

The number of stillbirths recorded was 373. A case was considered to be a stillbirth if the estimated length of gestation was 28 weeks or longer, irrespective of weight at birth. Table IX gives the causes of stillbirth in detail. In selecting asphyxia and intracranial haemorrhage as the primary cause of the stillbirth, the same criteria were used as in the classification of

TABLE IX. *Causes of Stillbirths.*

1. Erythroblastosis foetalis		6
2. Congenital defect		71
3. Asphyxia	53	
Asphyxia plus subdural haemorrhage	22	
Asphyxia plus subarachnoid and/or intraventricular haemorrhage ...	2	
Asphyxia plus intraperitoneal haemorrhage	1	
Asphyxia plus pneumonic changes ...	3	
	—	81
4. Subdural haemorrhage	7	
Subdural plus intraperitoneal haemorrhage	1	
Subdural plus subarachnoid haemorrhage	1	
Subdural haemorrhage plus slight asphyxia	2	
	—	11
5. Congenital syphilis	2	2
6. Other causes:		
Prematurity only	3	
Fractured spine	1	
Exsanguination	1	
	—	5
7. Intrauterine death with maceration		75
8. No autopsy: cause unknown		122
Total		373

deaths. Diagnosis was made on autopsy findings in 103 cases. Further diagnoses were made as follows:

Obvious congenital defect	61
Asphyxia diagnosed clinically	8
Intracranial haemorrhage diagnosed clinically following difficult delivery	3
Fractured spine diagnosed clinically	1

A definite diagnosis was thus obtainable in 176 cases. In a further 75 cases death occurred in utero before commencement of labour, a macerated foetus being produced. In 122 cases the pathological cause of death was not ascertained. Table X gives causes of stillbirth in relation to weight of foetus.

TABLE X.

Causes of Stillbirth by Birth-weight.

(*a*) *Numbers of cases.*	Below 3 pounds 9 ounces	3 pounds 9 ounces to 5 pounds 8 ounces	5 pounds 9 ounces to 8 pounds 15 ounces	Over 8 pounds 15 ounces	Total
Erythroblastosis foetalis	2	2	2	0	6
Congenital defects	34	16	19	2	71
Asphyxia	6	16	48	11	81
Subdural haemorrhage	0	2	6	3	11
Congenital syphilis	0	1	1	0	2
Other causes	3	1	1	0	5
Intrauterine death	25	17	28	5	75
No autopsy; cause unknown	21	31	64	6	122
Total	91	86	169	27	373
(*b*) *Percentages*					
Erythroblastosis foetalis	2.2	2.3	1.2	0.0	1.6
Congenital defects	37.4	18.6	11.2	7.4	19.0
Asphyxia	6.6	18.6	28.4	40.7	21.7
Subdural haemorrhage	0.0	2.3	3.6	11.1	2.9
Congenital syphilis and other causes ...	3.3	2.3	1.2	0.0	1.9
Intrauterine death	27.5	19.8	16.6	18.5	20.1
No autopsy: cause unknown	23.1	36.1	37.9	22.2	32.7
Total	100.0	100.0	100.0	100.0	100.0

1. *Causes of Stillbirth in Relation to Complications of Pregnancy.*

Table XI shows the presence or absence of complications of pregnancy in the mother in stillbirth due to various causes, in comparison with the incidence of complications in the mothers of babies who survived. The points to be noted are:

1. The high incidence of hydramnios occurring with congenital defects, the defect nearly always being anencephalus.

2. In cases of intrauterine death the toxaemia rate is twice as high as in the survivor group, and higher than that associated with any other cause of stillbirth or infant death. This suggests that maternal toxaemia may be an important aetiological factor in these cases.

3. In those stillbirths for which no pathological diagnosis of cause of death was made, the toxaemia rate was twice that of the survivor group, and the rate for antepartum haemorrhage was 6 times as high. Had autopsies been performed it is likely that where the mother had antepartum

TABLE XI.
Causes of Stillbirth by Complications of Pregnancy.

Cause of stillbirth	No complications per cent	Toxaemia per cent	Antepartum haemorrhage per cent	Hydramnios per cent	Others per cent	Total per cent
Congenital defects and erythroblastosis ...	40.3	9.1	9.1	32.5	9.1	100.0
Asphyxia	48.2	25.9	22.2	—	3.7	100.0
Subdural haemorrhage	81.8	18.2	—	—	—	100.0
Intrauterine death	56.0	34.7	4.0	—	5.3	100.0
Cause unknown ...	38.8	33.1	23.1	1.7	3.3	100.0
Survivors	69.2	17.1	3.0	1.1	9.6	100.0

haemorrhage the cause of death would have usually been found to be asphyxia.

4. The figures for subdural haemorrhage are based on only 11 cases, and no great importance can be attached to the apparently greater freedom from complications of pregnancy.

2. *Causes of Stillbirth in Relation to Mode of Delivery.*

Table XII shows the mode of delivery in stillbirths from specified causes, in comparison with a control group of babies who survived.

The category "subdural haemorrhage" in this Table covers all cases not specifically classified as "slight," including those in which the principal cause of the stillbirth was adjudged to be asphyxia. The main points to be noted are as follows:

1. The high incidence of breech delivery in all categories of stillbirth. The congenital defects occurring with breech delivery were mainly cases of hydrocephalus, microcephalus and anencephalus. Here the mode of delivery is most likely a consequence of the congenital defect. A similar consideration applies to cases of intrauterine death. In stillbirths due to asphyxia and subdural haemorrhage the high incidence of breech delivery is aetiologically important.

2. The high incidence of instrumental

TABLE XII.
Causes of Stillbirth by Mode of Delivery.

Cause of stillbirth	Spontaneous vertex per cent	Instrumental per cent	Breech per cent	Caesarean section per cent	Craniotomy per cent	Total per cent
Congenital defects and erythroblastosis ...	68.8	1.3	14.3	1.3	14.3	100.0
Asphyxia	50.8	17.4	20.6	7.9	3.2	100.0
Subdural haemorrhage (total)	20.7	44.8	27.6	6.9	0.0	100.0
Intrauterine death ...	63.9	5.3	14.7	1.3	14.7	100.0
Cause unknown ...	52.9	19.8	14.0	5.0	8.3	100.0
Survivors	78.2	13.4	4.6	3.8	0.0	100.0

delivery, amounting to 45 per cent of all cases, in stillbirths with subdural haemorrhage. Instrumental or breech delivery occurred in nearly three-quarters of the stillbirths from this cause.

Deaths and Stillbirths in Relation to Sex of Infant.

It was shown in the first paper in this series that although there is a higher prematurity-rate among females, male infants have a lower survival-rate, especially in the smaller weight groups. Table XIII gives the numbers of deaths and stillbirths and the rates per 1,000 total births by cause for male and female infants.

TABLE XIII.
Deaths and Stillbirths by Sex of Infant.

	Number of cases				Rate per 1,000 births	
	Male	Female	Unstated	Total	Male	Female
(*a*) *Deaths*						
Congenital defects	21	19	1	41	5.4	5.6
Erythroblastosis	11	5	—	16	2.8	1.5
Prematurity	28	9	2	39	7.2	2.6
Asphyxia	31	14	—	45	8.0	4.1
Subdural haemorrhage ...	5	3	—	8	1.3	0.9
Infections	32	13	2	47	8.3	3.8
Other causes	5	3	—	8	1.3	0.9
Total deaths	133	66	5	204	34.3	19.4
(*b*) *Stillbirths.*						
Congenital defects	27	40	4	71	7.0	11.8
Erythroblastosis	3	2	1	6	0.8	0.6
Asphyxia	48	31	2	81	12.4	9.1
Subdural haemorrhage ...	8	3	—	11	2.1	0.9
Intrauterine death	40	33	2	75	10.3	9.7
Intrauterine death	3	4	—	7	0.8	1.2
Cause unknown	67	54	1	122	17.3	15.9
Total stillbirths	196	167	10	373	50.7	49.2

The death-rate per 1,000 for female infants was 19.4 compared with 34.3 for males, giving a male excess of 14.9 per 1,000 births. The rate for congenital defects is approximately the same in the 2 sexes, but for every other cause of death the males had a higher rate. This is most marked in prematurity, asphyxia and neonatal infections. The sex-disparity becomes even more striking when account is taken of the effect of birth-weight. These causes of death tend to be more frequent in the smaller babies, but although the boy babies as a group are heavier than the girls, they show a considerably higher mortality.

The total stillbirth-rate is approximately the same for males and females. The female rate for congenital defects of 11.4 is 4.8 per 1,000 higher than the male rate, mainly because of the excess of cases of anencephaly among the females. For every other cause of stillbirth the males have a higher rate, though the disparity is not so great as in the case of deaths after delivery.

It would appear that female infants are the better able to withstand the hazards of

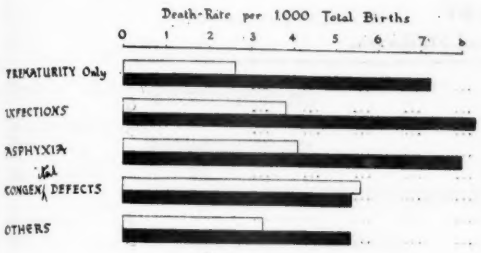

FIG. 3.
Death-rates according to sex.
Outlined rectangles—Females.
Black rectangles—Males.

the birth process and adaptation to a new environment than are male infants.

Death-rates for male and female infants from the main cause groups are shown in Fig. 3.

diagnosis. In this section an attempt is made to assess the primary cause of wastage. Each death and stillbirth has been considered separately, and all the factors influencing the outcome have been taken into account before a decision has been made on what comprised the primary and most important cause of the fatality. The findings for deaths are shown in Table XIV, and for stillbirths in Table XV, while Fig. 4 shows the main conclusions in graphical form.

It has already been shown in Part I how chances of survival depend largely on the weight of the infant at birth, and how the various complications of pregnancy predispose to premature labour. Where one

TABLE XIV.
Primary Causes of Death.

1. Congenital defects		41
2. Erythroblastosis foetalis		16
3. Prematurity (below 4½ pounds)		101
due to antepartum haemorrhage	15	
,, ,, ,, , death from asphyxia	16	
,, ,, ,, , death from infection	6	
due to toxaemia	18	
,, ,, , death from infection	6	
due to hydramnios	4	
due to early Caesarean section for acute abdomen	1	
Cause unknown, death from infection	10	
Cause unknown	25	
4. Asphyxia (over 4½ pounds)		15
due to antepartum haemorrhage	5	
,, ,, ,, , death from infection	2	
due to prolonged labour	3	
due to Caesarean section	1	
Cause unknown, associated with toxaemia	3	
accidental asphyxia	1	
5. Subdural haemorrhage due to birth trauma		12
Breech delivery	5	
Forceps delivery	5	
Manual rotation and forceps delivery	2	
6. Neonatal infection (over 4½ pounds)		18
7. Congenital syphilis		1
Total		204

Primary Cause of Wastage.

In previous sections the causes of death and stillbirth have been given by pathological findings at autopsy or on clinical

of these complications has resulted in the birth of a premature infant which did not survive, the primary cause is considered to the complication, irrespective of what

TABLE XV.

Primary Causes of Stillbirths.

1. Congenital defects		71
2. Erythroblastosis foetalis		6
3. Prematurity (below 4½ pounds)		85
due to toxaemia	39	
due to antepartum haemorrhage	22	
Cause unknown	24	
4. Postmaturity		3
5. Asphyxia (over 4½ pounds)		63
due to toxaemia	11	
due to antepartum haemorrhage	27	
associated with breech delivery	2	
,, ,, version and extraction	4	
,, ,, forceps delivery	1	
,, ,, Caesarean section	1	
,, ,, prolonged labour	10	
,, ,, ruptured uterus	1	
,, ,, true knot in cord	1	
Cause unknown	5	
6. Subdural haemorrhage		26
spontaneous vertex delivery with complications	4	
breech delivery	7	
version and extraction	8	
forceps, including failed forceps outside	7	
7. Hydramnios		2
8. Diabetes—intrauterine death		2
9. Congenital syphilis		2
10. No autopsy—associated with complications of delivery		53
complications necessitating craniotomy	22	
premature separation of placenta	1	
prolapsed cord	12	
prolonged labour	9	
contraction ring	2	
deep transverse arrest	5	
tonic uterine contractions	1	
fractured spine due to difficult delivery	1	
11. No autopsy—Cause unknown		60
associated with Caesarean section	1	
,, ,, forceps delivery	4	
,, ,, breech delivery	4	
,, ,, version and extraction	6	
,, ,, toxaemia and Caesarean section	2	
,, ,, ,, ,, forceps delivery	2	
,, ,, ,, ,, breech delivery	5	
,, ,, ,, ,, spontaneous vertex delivery	14	
spontaneous vertex delivery	22	
Total		373

was the pathological cause of death. Although the upper limit of prematurity is generally taken to be 5½ pounds, the larger premature infants stand a good chance of surviving. It was therefore decided to assume that for infants of 4½ pounds or less the presence of the prematurity itself was likely to be the most important factor in causing death or stillbirth, but between 4½ and 5½ pounds some other factor such as infection or birth trauma would be the more decisive in cases that did not survive. For

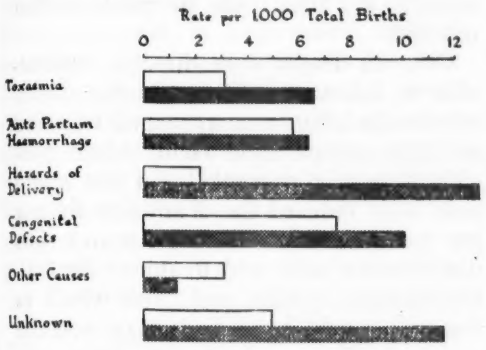

FIG. 4.
Primary causes of wastage.
Outlined rectangles—Deaths.
Black rectangles—Stillbirths.

example, Table XIV lists 10 cases of deaths from infection in infants below 4½ pounds, in whom the cause of prematurity was unknown. These cases are considered to be known". On the other hand, among the 18 cases under the heading "neonatal infection", there were a number of cases between 4½ and 5½ pounds, the primary cause in these instances being regarded as infection rather than prematurity.

In the deaths a definite decision could be made in every case. Among the stillbirths, owing to the much smaller proportion of autopsies, this was not always possible. In 53 of the cases for which autopsy was not performed, there was some complication of delivery of sufficient severity to be a likely cause of stillbirth. In the remaining 60 cases without autopsy, the diagnosis of cause of stillbirth is doubtful. Fifteen were delivered by the breech, forceps or Caesarean section, and it is possible that the mode of delivery was responsible for the stillbirth. Nine more

TABLE XVI.
Primary Causes of Wastage.

Cause of wastage	Numbers of cases.			Percentages			Per 1,000 births		
	Deaths	Still-births	Total	Deaths	Still-births	Total	Deaths	Still-births	Total
Congenital defects	41	71	112	20.1	19.0	19.4	5.4	9.3	14.7
Erythroblastosis	16	6	22	7.8	1.6	3.8	3.1	6.6	9.7
Toxaemias	24	50	74	11.8	13.4	12.8	2.1	0.8	2.9
Antepartum haemorrhage	44	48	93	21.6	13.1	16.1	5.8	6.4	12.2
Hydramnios	4	2	6	2.0	0.5	1.0	0.5	0.3	0.8
Neonatal infection	18	—	18	8.8	—	3.1	2.4	—	2.4
Congenital syphilis ...	1	2	3	0.5	0.5	0.5	0.1	0.3	0.4
Diabetes	0	2	2	0.0	0.5	0.3	0.0	0.3	0.3
Postmaturity	0	3	3	0.0	0.8	0.5	0.0	0.4	0.4
Hazards of delivery ...	17	99	116	8.3	26.5	20.1	2.3	13.0	15.3
Accidental asphyxia ...	1	0	1	0.5	0.0	0.2	0.1	0.0	0.1
Possible cause:									
Toxaemias	3	14	17	1.5	3.8	2.9	0.4	1.8	2.2
Toxaemia plus hazards of delivery	0	9	9	0.0	2.4	1.6	0.0	1.2	1.2
Hazards of delivery ...	0	15	15	0.0	4.0	2.6	0.0	2.0	2.0
Cause unknown	35	51	86	17.2	13.8	14.9	4.6	6.7	11.3
Total	204	373	577	100.0	100.0	100.0	26.8	49.1	75.9

primarily deaths from prematurity, and not from infection, and as the cause of prematurity is not known, they are classified in Table XVI under "cause unknown". On the other hand, among the 18 cases under the heading "neonatal infection", there were a number of cases between 4½ and 5½ pounds, the primary cause in these instances being regarded as infection rather than prematurity.

In the deaths a definite decision could be made in every case. Among the stillbirths, owing to the much smaller proportion of autopsies, this was not always possible. In 53 of the cases for which autopsy was not performed, there was some complication of delivery of sufficient severity to be a likely cause of stillbirth. In the remaining 60 cases without autopsy, the diagnosis of cause of stillbirth is doubtful. Fifteen were delivered by the breech, forceps or Caesarean section, and it is possible that the mode of delivery was responsible for the stillbirth. Nine more came of mothers with toxaemia of pregnancy, as well as having an abnormal delivery. A further 14 cases from toxaemic mothers had a spontaneous vertex delivery,

with no complicating factors. There were 22 cases with a normal delivery, and no accompanying abnormalities either during pregnancy or labour; for these the cause of stillbirth is quite unknown.

Table XVI shows the primary causes of death and stillbirth, as given in Tables XIV and XV, classified into 11 groups with a further 3 groups where a possible cause is suggested. It is seen that congenital defects plus erythroblastosis are responsible for nearly 24 per cent of all deaths and stillbirths, toxaemia and antepartum haemorrhage in the mother for 30 per cent, hazards of delivery for 20 per cent, while all other causes account for only 6 per cent. In 22 per cent of the cases the cause of wastage was unknown.

Prospects of Reduction of the Stillbirths and Neonatal Death-rate.

In considering the results of the investigation on the prospect of further reducing stillbirth and infant death-rates, the problem can be approached from the following four angles:

1. *Postnatal Measures.*

Postnatal care of the infant may be directed to special treatment of premature babies, prevention of infection, and the treatment of trythroblastosis foetalis. The premature babies in this series of cases were nursed under excellent conditions in air-conditioned incubator-rooms, under the supervision of paediatricians and nurses experienced in the care of very small babies. Comment has already been made on the fact that no further improvement in treatment appears to be of much avail in saving premature infants who die within 48 hours of birth, and it seems unlikely that the death-rate of the minority who survived to die later could be much further reduced.

Only 18 deaths were directly attributable to infection. These deaths, which occurred in infants over 4½ pounds who had no other complicating factor might possibly have been prevented, but that would only have reduced the death-rate by 2.4 per 1,000 births. Recent research has discovered a cause and treatment for erythroblastosis foetalis, and cases which in the past would have died, may now be saved. But here again the cases form only a small proportion of the total wastage-rate. In short, at the best the reduction of the neonatal death-rate that is possible by postnatal measures can deal only with a fraction of the problem.

2. *Measures During Labour and Delivery.*

Death amounting to 2.2 and stillbirths to 13 per 1,000 births were attributed to hazards of delivery, this being about one-fifth of the total wastage. Many of these cases were admitted as emergencies, and might have been saved given more adequate antenatal supervision with early diagnosis and correction of abnormalities.

3. *Measures During or Before Pregnancy.*

Abnormal conditions in the mother, toxaemia of pregnancy and antepartum haemorrhage, accounted for nearly one-third of the total wastage. A reduction in the incidence of these 2 conditions would lead to a substantial lowering in the infant death- and stillbirth-rates. Maternal death-rates from these complications have fallen since 1939, and this may be taken as an indication of lowered case-incidents. Though this fall may be due in part to better antenatal care, it is probable that it is largely the result of better nutrition of mothers during the war. It is hoped in a further paper to deal with the effect of

social and economic factors on prematurity. There is already a considerable body of evidence on the important effect of such factors as housing, nutrition, employment of pregnant women and poverty on infant death- and stillbirth-rates, as for example in the papers by Woolf and Waterhouse (1945) and Baird (1945).

4. *Conditions at Present not Amenable to Treatment.*

Nearly one-fifth of the total wastage was due to congenital defects. In the present state of our knowledge these deaths are not preventable, though a new line of research was opened up by Gregg (1941), when he described an association between maternal infection during the early months of pregnancy and defect in the infant. This is a field which should amply repay further investigations.

Summary.

This paper comprises Part III in a series of studies based on nearly 8,000 births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive, and deals with deaths and stillbirths.

Recorded deaths were 204, 142 in premature and 62 in mature infants. Of the 373 stillbirths, 177 were premature and 195 were mature or postmature. Nearly one-quarter of the premature deaths took place in the first 6 hours and one half on the first day; 25 per cent of mature deaths occurred during the first day.

Among premature infants the commonest causes of death were prematurity alone, asphyxia and pneumonia, while congenital defects accounted for the majority of the mature deaths. Congenital defects and asphyxia were the commonest pathological findings in stillbirths for both premature and mature infants, but in over half the cases there was no pathological diagnosis. There was a much higher incidence of complications of pregnancy in the mothers of babies who died as compared with those who survived. The same is true for abnormal forms of delivery. A detailed analysis of these cases is given according to the nature of complication or method of delivery and pathological cause of death or stillbirth.

Death-rates for congenital defects are about the same for males and females but for every other cause boys show a higher rate. Females have a higher stillbirth-rate from congenital defects, mainly due to excess anencephalus, but males have a higher rate from every other cause. Total rates per 1,000 births were:

Deaths: males 34.3; females 19.4.

Stillbirths: males 50.6; females 49.1.

Intracranial haemorrhage was found at autopsy in 65 out of the 204 infant deaths. Subdural haemorrhage was commonest in larger babies and, unless mild, associated with birth trauma. Subarachnoid, intraventricular and intracerebral haemorrhage occurred almost exclusively in prematures, and was associated with asphyxia.

There was a rise in the death- and stillbirth-rate from congenital defects with increasing maternal age.

An attempt has been made to assess what was the primary cause of each case of death or stillbirth. Of total cases of wastage: 24 per cent were attributed to congenital defects; 13 per cent to toxaemias of pregnancy; 16 per cent to antepartum haemorrhage; 20 per cent to hazards of delivery; 6 per cent to all other causes.

Finally, suggestions have been made, based on the above results, of possible ways of reducing stillbirth- and neonatal death-rates.

It is a pleasure to thank Professor C. McNeil and Mr. W. F. T. Haultain for permission to use pediatric and obstetrical records; Mrs. W. Lord, B.A., and Miss Joyce Thomson for assistance in the analyses and computations; Dr. Barnet Woolf for advice on the planning of the investigation and on the statistical methods used: Dr. Agnes Macgregor for permission to quote from autopsy findings; Professor McNeil and Professor R. W. B. Ellis for their interest and encouragement.

REFERENCES.

Baird, D. (1945): *J. Obstet. and Gynec.*, **52**, 217, 339.

Blackfan, K. D., and Yaglou, C. P. (1933): *Amer. J. Dis. Child.*, **46**, 1175.

Clifford, S. H. (1934): *J. Pediat*, **5**, 139.

Drillien, C. M. (1947a): *J. Obstet. Gynaec.*, **54**, 300.

Drillien, C. M. (1947b): *J. Obstet. Gynaec.*, **54**, 443.

Gregg, N. M. (1941): *Trans. Ophthalm. Soc. Aust.*, **3**, 35.

Malpas, P. (1937): *J. Obstet. Gynec.*, **44**, 443.

Penrose, L. S. (1946): *Ann. Eugen.*, **13**, 73.

Woolf, B., and Waterhouse, J. (1945): *J. Hyg., Camb.*, **44**, 67.

A Further Contribution to the Study of the Influence of Failure of Müllerian Duct Fusion on Pregnancy and Labour

BY

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IN 1945 I published a paper on this subject describing the effects of minor uterine deformities on pregnancy and labour in 18 patients. In that paper I drew attention to several important facts. Firstly, these deformities are more common than textbooks would lead one to think. Secondly, they expose the mother and foetus to certain hazards, many of which can be guarded against if the deformity is recognized. Thirdly, the chief of these abnormalities is transverse lie, repeated abortions and an increased risk of retention of the placenta. At the time of writing that paper I desdescribed 3 women who were then undelivered. Since that time I have seen 19 further cases, and the object of this paper is to give their clinical histories and review the 78 pregnancies which these 37 patients had between them.

Cases 16, 17 and 18 were described in my previous paper but were delivered after its publication. It is sufficient here to describe the ultimate outcome of these 3 cases.

CASE 16. This patient had a normal delivery and was found to have a uterus bicornis unicorpus unicollis.

CASE 17. This patient had a normal delivery and also had a uterus bicornis unicorpus unicollis.

CASE 18. Premature labour at 34 weeks. Child an anencephalic monster. Here again the patient had a uterus bicornis unicorpus unicollis.

In the year that followed the publication of my first paper I met with 19 further examples of this deformity. There was no special selection of cases in this series and 15 of them were discovered among 1,200 routine cases in the antenatal clinic. This is an incidence of 1 in 78 cases. This apparent increased incidence was undoubtedly due to the fact that we were looking for them and I think there can be few that escaped our notice. Sometime ago, when visiting another maternity hospital, the resident obstetrician showed me some antenatal cases and one of these presented the typical uterine deformity. These findings lend support to my previous statement that they are relatively common.

CASE 19. Age 31; 2 gravida.

Pregnancy 1. Normal delivery of a 9 pounds infant.

Pregnancy 2. At 36 weeks uterine deformity was noticed and the baby was presenting as a breech. In the circumstances version was not attempted. The membranes ruptured 4 days before the onset of pains. A normal breech delivery took place after 12 hours of labour. The placenta was retained and there was a severe postpartum haemorrhage. Crede's expression of the placenta was done. Good recovery. Male child weighing 7 pounds 7½ ounces.

CASE 20. Age 29; 1-gravida.

Pregnancy 1. Repeated transverse lie throughout the antenatal period. Version was performed many times but the transverse lie always recurred. The day before labour commenced spontaneous cephalic version took place and the patient had

a normal delivery. The placenta was retained for 2½ hours but there was no haemorrhage. Living female child weighing 8 pounds 7 ounces.

CASE 21. Age 41; 2-gravida.

Pregnancy 1. Normal delivery of a 9½ pounds baby 12 years prior to the second pregnancy.

Pregnancy 2. Uterine deformity diagnosed 6 weeks before term. Repeated transverse lie throughout the last 4 weeks of pregnancy. Spontaneous version the day before labour commenced. Vertex presentation and normal delivery of a living male child weighing 7 pounds 8 ounces. Placenta retained for 1 hour 10 minutes, but there was no haemorrhage.

Whilst congratulating myself on the results of my conservatism in this case (I had been urged by a colleague to perform Caesarean section) I had no forewarning of the sequel which was nearly to cost the patient her life. Despite the fact that the puerperium was normal and that the lochia stopped on the 10th day, a small portion of a cotyledon of placenta was retained and was overlooked at the routine examination following the third stage. Three weeks after discharge she was re-admitted with a small secondary postpartum haemorrhage. I curetted this patient and found organizing placental remnants in the right cornu firmly adherent to the uterine wall. As soon as I dislodged some of the fragments a torrential haemorrhage began. I was unable to reach the cornu with a finger or to remove all the fragments with the curette. In 10 minutes, despite packing the uterus, this patient lost 6 pints of blood, excluding clots. The collapse associated with this tremendous bleeding was very severe and the patient was soon *in extremis*. Transfusion was started in all 4 limbs at once, and under pressure 8½ pints of blood were transfused in 14 minutes. In view of the patient's age I had no hesitation in performing subtotal hysterectomy and by this means the bleeding was controlled. Altogether she received 15 pints of blood in 4 hours (10 of them in the first 25 minutes) and by the end of the operation her pulse-rate was 130 and her blood-pressure 70/40. To digress for a moment, I would like to stress the importance of rapid transfusion in cases of rapid loss of blood such are encountered in midwifery. The object is to restore the blood volume to normal as rapidly as possible and where active bleeding is taking place there is no danger of overloading the circulation by rapid transfusion. If a patient can lose 6 pints of blood in 10 minutes (and this quantity was measured and not guessed) to replace this by transfusing 1 pint in half-an-hour is obviously futile.

This patient made an excellent recovery from her operation and has remained well since. The specimen showed a uterus bicornis unicorpus unicollis with small placental fragments densely adherent to the right cornu and the placental site showed a large number of patent veins in its base.

CASE 22. Age 22; 2 gravida.

Lobectomy for bronchiectasis at the age of 10. Bronchiestasis of opposite lung.

Pregnancy 1. Normal delivery of 7½ pounds child.

Pregnancy 2. Admitted in labour at 32 weeks with transverse lie and prolapsed hand. Obvious uterine deformity. Patient's general condition poor. Internal version and delivery of a stillborn female child weighing 4 pounds 10 ounces. Placenta retained for 1 hour. Postpartum haemorrhage then commenced which was checked at once by Crede's expression of the placenta. During the course of the version the placenta was found situated in the right cornu.

An autopsy was performed on the baby and its uterus was found to be, like its mother's, a uterus bicornis unicorpus unicollis very similar to the one I illustrated in my first paper.

CASE 23. Age 21; primigravida.

Patient attended the antenatal clinic where the deformity was diagnosed at the 20th week. The presentation was vertex throughout pregnancy and the head engaged at the 36th week. Normal delivery of a living female child weighing 6 pounds 4 ounces. The placenta was retained for 2 hours with severe postpartum haemorrhage. Manual removal of placenta which was situated in the right horn was done. There was delay in removing this placenta and the haemorrhage necessitated a blood transfusion.

CASE 24. Aged 34; 3-gravida.

Pregnancy 1. Abortion at 3 months.

Pregnancy 2. Abortion at 3 months.

Pregnancy 3. Uterine deformity noticed at 33rd week; presentation vertex. Normal labour and

normal delivery of a female child weighing 6 pounds 14 ounces. Third stage normal.

CASE 25. Aged 23; primigravida.

Uterine deformity noticed at 16 weeks. Presentation vertex throughout pregnancy. Patient had mitral stenosis and aortic regurgitation. Normal delivery of a female infant weighing 5 pounds 8 ounces. Third stage normal.

CASE 26. Aged 33; 6-gravida.

Pregnancy 1. Normal vertex; 7 pounds.
Pregnancy 2. Breech; 6½ pounds.
Pregnancy 3. Breech; 10 pounds.
Pregnancy 4. Vertex; 5½ pounds.
Pregnancy 5. Vertex 10 pounds.
Pregnancy 6. Admitted to hospital as an emergency in labour suffering from antepartum haemorrhage. On examination the uterus showed a well-marked fundal deformity, the child presented by the shoulder; there was a marginal placenta praevia present covering half of the os, which was three-quarters dilated. The fundus of the uterus was in tonic contraction. I decapitated the infant (a female weighing 6 pounds 14 ounces), delivered her and removed the placenta manually. This was an example of uterus bicornis unicorpus unicollis. The infant's uterus was normal. The right horn in this case was longer than the left.

CASE 27. Age 25; 2-gravida.

Pregnancy 1. Normal delivery: child's weight 7½ pounds.

Pregnancy 2. At 37 weeks the uterine deformity was noted and the baby presented as a breech. Version was unsuccessful. At term the patient was admitted in labour with an oblique breech presentation. After 8 hours in labour the membranes ruptured at full dilatation and the cord prolapsed. Immediate breech extraction of a living female infant weighing 6 pounds 9 ounces. The head of this foetus was in the left horn of the uterus as was also the upper margin of the placenta. The remainder of the placenta lay on the posterior wall and the lower border almost reached the lower segment. The third stage was normal and lasted only 10 minutes.

CASE 28. Aged 28; 2-gravida.

Pregnancy 1. Premature labour at 30 weeks.

I operated on this patient for a ruptured ectopic gestation and performed a left salpingectomy. There was a depression at the fundus which was well marked even though the uterus was not greatly enlarged.

CASE 29. Age 23; 2-gravida.

Pregnancy 1. Abortion at 3 months.

Pregnancy 2. First seen at 39 weeks. Obvious uterine deformity and a transverse lie. Version attempted without anaesthesia but failed. At term version under anaesthesia failed to correct the transverse lie. Labour commenced and the transverse lie still could not be corrected. Lower segment Caesarean section was done and a living female child weighing 6 pounds was born. The placenta was on the posterior and left lateral walls but did not reach to the lower segment.

CASE 30. Age 30; 2-gravida.

Pregnancy 1. Normal delivery of 6 pounds baby after trial labour for persistent non-engagement of the head.

Communication with the hospital where this delivery took place showed that the deformity had not been recognized.

Pregnancy 2. At 34 weeks the deformity was very obvious and the baby lay as an oblique breech. Version failed. At 36 weeks the presentation was transverse. At 38 weeks it was again an oblique breech. Version under anaesthesia failed. Lower segment Caesarean section was done at term. A living male child weighing 8 pounds was born. The placenta lay on the right lateral wall and reached almost to the lower segment. This patient was a sister of Case 7 described in the previous series.

CASE 31. Age 30; 2-gravida.

Pregnancy 1. Abortion at 8 weeks.

Pregnancy 2. Threatened abortion at 8 weeks and again at 12 weeks. The abnormal uterine contour became obvious at 24 weeks. Toxaemia at term. Vertex presentation. Induction of labour. Stillborn male child. Placenta retained with slight haemorrhage and severe obstetric shock; treated by blood transfusion. Manual removal of placenta, which was situated on the right lateral wall, in the cornu and slightly on the septum. Good recovery.

CASE 32. Age 24; primigravida.

This patient was the wife of an American soldier and was brought to me by her mother when she was 24 weeks pregnant. The patient wished to

join her husband in America and her mother wanted her to stay in England until the baby was born. The reason for this was that the mother had had "such terrible times with her babies" that she was convinced the same fate would befall her daughter. This idea was strengthened by the fact that her eldest daughter had lost her life in childbirth. The patient was 24 weeks pregnant with a very obvious uterine deformity and a transverse lie.

The mother was a communicative woman and told me that at each of her 11 labours she "had one foot in the grave and that she had sent her family doctor prematurely to his death by the worry of her repeated abnormal pregnancies." The latter part of this statement was the more regretable, in that he was thus unable to give me valuable information about the true obstetric history of this woman. However, I did interview the handywoman who had attended some of her labours with the doctor and after a stern cross-examination in which I tried to eliminate all romancing it seemed likely that this woman had had placenta praevia on 3 occasions, postpartum haemorrhage on 4 others and one "turning-operation to bring the baby." I tried to persuade her to let me put lipiodol into her uterus but she refused. I obtained a copy of her eldest daughter's death certificate and the certified cause of death was "antepartum haemorrhage and shock due to placenta praevia—internal version". The doctor who signed this certificate is now also dead. It seems probable that the mother and both her daughters had this uterine deformity. I advised my patient to stay at home until she was delivered, but she refused my advice and went to America. I have tried to find out the outcome of her pregnancy, but I have not received replies to my letters and the mother is apparently so frightened that I will again suggest putting lipiodol into her uterus that she will not come to see me.

CASE 33. Age 23; primigravida.

Pregnancy 1. Repeated transverse lie throughout pregnancy. Version was attempted twice and malpresentation recurred each time. Labour at term and foetus remained transverse. Lower segment Caesarean section done. Living male child weighing 7 pounds. Placenta on right lateral wall and in right cornu.

CASE 34. Age 20; primigravida.

Pregnancy 1. Normal pregnancy and labour; vertex presentation. Placenta retained 2 hours with postpartum haemorrhage treated by manual removal. Placenta in left cornu.

CASE 35. Age 23; primigravida.

Pregnancy 1. Normal pregnancy; vertex presentation, persistent occipito-posterior. Manual rotation and forceps delivery at term. Third stage normal.

CASE 36. Age 27; primigravida.

Pregnancy 1. Normal pregnancy and labour, vertex presentation. Retained placenta with postpartum haemorrhage treated by manual removal. Placenta in right cornu.

CASE 37. Age 66; 1-para.

This patient was referred to me at the cancer clinic for postmenopausal haemorrhage. She had had one normal pregnancy and delivery. I found that the fundus of the uterus contained a carcinoma and I performed a panhysterectomy. The uterus proved to be a well-marked example of uterus bicornis unicorpus unicollis, with a pedunculated adenocarcinoma growing from the apex of the septum. No other part of the uterine wall was involved in the growth, which was the size of a walnut.

All the uteri in this series were of the variety which I designated uterus bicornis unicorpus unicollis. In the first series there were 5 cases of uterus subseptus and 5 of uterus bicornis unicorpus unicollis and 1 which it was impossible to classify accurately as only the shape of the cavity was known. In the whole series the classification is therefore:

Uterus bicornis unicorpus unicollis	31
Uterus subseptus	5
Unclassified	1
Total	37

Table I shows a summary of the 78 pregnancies of which details are known and Table II shows the type and number of abnormalities which occurred in these 78 pregnancies.

TABLE I.

Case	Pregnancy 1	2	3	4	5	6
1.	Transverse stillborn	Transverse placenta praevia	Transverse			
2.	Premature transverse to breech	Transverse presentation of cord Placenta praevia				
3.	Abortion	Normal delivery, retention of cotyledon of placenta	Normal delivery	Abortion	Transversed retained placenta	Normal Oblique to vertex (spontaneous)
4.	Abortion	Transverse Retained placenta				
5.	Premature vertex stillborn	Transverse prolapsed cord				
6.	Premature twins, both breech.	Forceps delivery	Twins Breech and foetus compressus	Breech		
7.	Transverse to vertex	Transverse				
8.	?	Transverse	Transverse			
9.	Abortion					
10.	Abortion	Transverse				
11.	Abortion	Abortion	Abortion	Abortion	Abortion	
12.	Abortion	Abortion				
13.	Transverse					
14.	Vertex					
15.	Vertex placenta praevia					
16.	Vertex	?	Abortion	Abortion	Abortion	Vertex
17.	Vertex					
18.	Vertex	Vertex	Premature vertex			
19.	Vertex	Breech P.P.H.				
20.	Transverse to vertex P.P.H.					
21.	Vertex	Transverse to vertex P.P.H.				
22.	Vertex	Premature Transverse Prolapsed cord retained placenta				
23.	Vertex P.P.H. retained placenta					

TABLE I (*Continued*)

Case	Pregnancy 1	2	3	4	5	6
24.	Abortion	Abortion	Vertex			
25.	Vertex	Breech	Breech	Vertex	Vertex	Transverse placenta praevia
26.	Vertex					
27.	Vertex	Transverse to breech Prolapsed cord				
28.	Premature vertex	Ectopic				
29.	Abortion	Transverse				
30.	Vertex	Transverse				
31.	Abortion	Vertex retained placenta P.P.H.				
32.	(Transverse)*					
33.	Transverse					
34.	Vertex retained placenta P.P.H.					
35.	Vertex					
36.	Vertex retained placenta P.P.H.					
37.	Vertex					

* At 24 weeks. Patient lost sight of and outcome unknown.
Case 7 and Case 30 were sisters.

TABLE II.
Complications of Pregnancy and Labour.

Number of patients, 37.
Number of pregnancies, 78.

Transverse lie	21 (27 per cent)
Abortion	19 (26 per cent)
Retained placenta	12 (15 per cent)
Breech	7 (9 per cent)
Premature labour	7 (9 per cent)
Placenta praevia	4 (5 per cent)
Prolapse of cord	4 (5 per cent)

As in my previous series transverse lie was the commonest abnormality seen in these cases. Some of them underwent spontaneous version even as late as the commencement of labour. It is obvious therefore that the routine employment of Caesarean section in these patients is unnecessary and is to be deprecated. I now allow the patient to go to term in every case. If the baby is very large or cannot be moved from the transverse by attempts at version then I perform Caesarean section at the onset of labour; in other cases I allow labour to proceed as spontaneous version often takes place in the first stage. If it does not, provided the membranes can be retained intact for long enough, internal version can be used as an alternative. As soon as the membranes rupture the patient must be examined vaginally. If the os is more than half dilated internal version is indicated. If it is not or the cord has prolapsed there should be a very strong contra-indication to deter the operator from performing Caesarean section.

In all these cases I perform examination under anaesthesia before attempting version, owing to the likelihood of meeting with placenta praevia.

Abortion.

There seems no reason to alter the remarks that I made in my previous paper. I urged the radiological examination of the uterus in cases of repeated abortion, and where the syndrome is definitely the result of the deformity operative correction is called for. This is perhaps the most difficult aspect of the subject upon which to give advice conscientiously. Two abortions or even 3 may be followed by an uneventful pregnancy. The operation is not an easy one and the risks of rupture of the scar in a subsequent pregnancy must be remembered, especially as the scar must of necessity be placed in a very unfavourable position, namely the uterine fundus.

Postpartum Haemorrhage.

In this second series (Cases 16 onwards) the greatest conservatism was practised in the conduct of the third stage. Despite this, retention of the placenta occurred in 9 cases and there was postpartum haemorrhage in 5. In 2 of these the haemorrhage was very severe. This was due to the reluctance of a junior medical officer to manually remove the placenta quickly enough. Conservatism is, of course, correct, but at the first sign of free bleeding there should be no delay in attempting Crede's manoeuvre and, if it fails, in following it immediately by manual removal.

I stated in my previous paper that all patients with this deformity should be delivered in hospital. One of the strongest reasons for this statement is the liability of these patients to develop difficulties in the third stage. Manual removal of the placenta is a serious operation even under ideal conditions. In domiciliary midwifery it is in the majority of cases positively dangerous. Since by palpation most of these cases can be recognized at antenatal examination there is no reason why they should not be admitted for their labour to a hospital where blood transfusion is available and asepsis and antisepsis easily achieved.

Placenta Praevia.

In the earlier series it seemed that this deformity favoured placenta praevia and this is supported by fresh evidence. A review of the literature reveals papers describing this deformity in women who had placenta praevia in successive pregnancies. Schwarz, in 1891, described such a patient who had 3 successive pregnancies with placenta praevia on each occasion. Fifty years later Andrews and Nicholls (1941) of Norfolk, U.S.A., described another case. Their patient suffered from placenta praevia in each of her 3 confinements. At the third she was delivered by Caesarean section. They describe the uterus as having a septum which projected into the cavity and a dimple on the external surface, but they do not seem to associate the deformity with the occurrence of the placenta praevia. The remainder of the literature, such as it is, on the subject of placenta praevia in repeated pregnancies makes no mention of uterine deformities nor is there any evidence to show that the authors ever looked for such a cause.

Prolapsed Cord.

It is not surprising that this complication should be seen since transverse lie (itself a condition predisposing to prolapsed cord) is seen so frequently. It is obviously a secondary effect of the deformity.

Inheritance of the Deformity.

Once again in this series I found a stillborn offspring of one of the mothers to have a uterus bicornis unicorpus unicollis. In addition Case 7 and Case 30 were sisters, and in Case 32 it is likely that this patient's mother had the deformity and possibly also her elder sister.

Carcinoma of the Uterus.

The last case described was discovered accidentally at an operation for uterine carcinoma. The literature contains quite a number of such case reports and specimens of such are not infrequently seen in museums. It is possible that a great many of these cases find their way into museums because of their "specimen appeal" but it would be interesting to know if there is a true increase in the incidence of carcinoma in malformed uteri.

SUMMARY.

1. A further 19 cases of minor degrees of failure of fusion of the Müllerian ducts are described.

2. The details of 78 pregnancies are given.

3. The commonest complications observed were transverse lie (27 per cent), abortion (26 per cent) and retained placenta (15 per cent). The management of these is discussed.

4. A plea is made for the detection of these cases during the antenatal period and for their delivery in hospital.

REFERENCES.

Andrews, C. J., and Nicholls, R. B. (1941): *Amer. J. Obstet. and Gynec.*, **42**, 538.

Schwarz (1891): *Cbl. Gynäk.*, **15**, 1060. (Abstr. in *Brit. med. J.*, 1892), **1**, *Epit. Curr. Lit.*, 10.

Way, S. (1945): *J. Obstet. Gynaec.*, **52**, 325.

Angular Pregnancy at Term complicated by Constriction Ring

BY

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ANGULAR pregnancy progressing to term is a rare phenomenon (DeLee, 1940b; Kerr, 1944b).

Constriction ring is an uncommon complication of labour (Gibberd, 1938).

A combination of these conditions—if the diagnosis be correct—together with partial destruction of the affected uterine muscle and lipiodol leakage into the pelvic veins (when, during convalescence, attempts were made to demonstrate the remaining uterine cavity) makes this case sufficiently interesting to warrant publication.

Mrs. C. J., 27 years old, Cape coloured, 4-para, was admitted at 4 p.m. on July 11th, 1946, being sent into hospital by her doctor as a "Tonic contraction of the uterus."

History.

Past. 1932, aborted when 3 months pregnant. 1942, normal pregnancy, delivery and puerperium, at term. 1945, normal pregnancy, delivery and puerperium, at term. These deliveries took place at home. Both her children are alive.

Present. The patient states that she did not attend an antenatal clinic.

Up to July 4th, 1946, she was perfectly well and carried on with her household duties as usual. The following day she noticed that all foetal movements had ceased. On July 6th she experienced a dull backache and lower abdominal cramps, that is, like the onset of a normal labour. During the day her membranes ruptured. On July 7th she had slight infrequent, irregular labour pains. The pains passed off after about 12 hours. Towards evening she felt slightly feverish. Since July 8th she had had more or less continuous dull abdominal pain. At odd intervals a little blood escaped from her vagina. On the 10th dark evil-smelling "clots" were passed vaginally. Although she felt ill she was not confined to bed.

Since July 11th she had felt really ill, being more feverish than before. She was too ill to get out of bed. She now noticed small fine hair in the vaginal discharge. She sent for a doctor. He examined her vaginally and sent her into hospital.

On Examination.

General. The patient looked very ill. There were sordes on her lips and her tongue was dry. Temperature, 100.8°F.; pulse, 160; respirations, 35; blood-pressure, 115/90 mm.Hg.

Local.

Abdomen. The abdomen was grossly distended. The fundus was up to the ensiform cartilage. The uterus was tense and tender. No gut was felt lying anterior to the uterus. The lie of the child could not be determined. Palpation revealed a peculiar crackling sensation over the uterus. The uterus was resonant to percussion. The foetal heart was not heard.

Vaginal examination. There was a foul-smelling, bloody-purulent vaginal discharge. A swab was taken for bacteriological examination. The os admitted 2 fingers. Separating the os from the head was a cylindrical channel about 1½ inches long, admitting 1 finger only. The membranes were found to be ruptured and scalp was protruding through both the narrow channel and cervix. The head was presenting. Bare bone was palpated. The upper end of the constricted channel was tightly applied to the head. The head was pushed up in order to allow gas to escape. The gas was foul smelling. Foetal hair was present on the examining finger.

Urine. Orange colour, specific gravity, 1014; trace of albumen; no sugar or acetone.

X-ray (straight-portable), *vide* Fig. 1. Postero-anterior and lateral views taken to show the gas within the uterus.

Treatment. Antigasgangrene serum, penicillin, sulfadiazine, intravenous saliine and glucose followed by 2 pints whole blood given.

11 p.m. There was slight improvement in the clinical picture. There were no uterine contractions. Vaginal examination made to let out more gas. There was no change in the state of either the cervix or the ring.

July 12th, 1946. 3 a.m. The patient had a rigor. 5 a.m. Abdominal distension had increased. Vaginal examination made to release gas. There was no change either in cervix or ring. 6 a.m., castor oil 2 ounces per os; 8 a.m., hot enema; 10 a.m., pituitrin, m. 3 given intramuscularly, quinine gr. 1 per os; 11 a.m., 12 noon, 1 p.m., pituitrin and quinine repeated.

As there were no uterine contractions (objectively) and as the patient's condition now started deteriorating—her pulse-rate increasing with a severe drop in temperature—hysterectomy was decided upon.

The diagnosis was (1) Foetal death and putrefaction. (2) Paralysis or death of the uterine muscle. (3) Puerperal infection (? Gas gangrene).

Preliminary bacteriological report: "Large gram-positive bacilli present in fair numbers, various sizes, some filamentous, others tending to form chains. Few showing enlarged terminal spores."

Blood transfusion was started again in order to continue throughout and after the operation (3 pints were given). As it was not clear whether a subtotal could be done, the patient was prepared for a total hysterectomy.

Operation.

July 12th, 1946, 2 p.m. The vagina was cleared and the external os was stitched after a plug was inserted into the uterus. The abdomen was opened by means of a midline incision extending from 2 inches above the umbilicus to 1 inch above the symphysis pubis. On opening the abdomen omentum was found to be adherent to the fundus and anterior surface of the uterus. It was also adherent to the peritoneum of the anterior abdominal wall. The upper segment was greenish-purple in colour, extremely thin, and stank. The lower segment appeared normal. There was no clear line of demarcation. A subtotal hysterectomy was therefore decided upon. Omental adhesions were stripped where possible and severed and tied where the latter was impossible When the anterior wall and fundal adhesions were cleared the uterus was lifted out of the abdominal cavity only to find that gut was adherent to its posterior wall. These adhesions were now freed. Once lifted out of the abdominal cavity the uterus was well packed off with swabs.

A subtotal hysterectomy was done in the usual way. The essential differences were that the vessels on the right side—both uterine and ovarian, were grossly enlarged. The lower segment was friable. In order to avoid intra-peritoneal spilling the lower segment was severed between clamps. The amputation was at a higher level than reached by the plug inserted before the abdominal operation. The uterine stump was covered with peritoneum. A drainage tube was inserted. The abdomen was closed in the usual way.

20 ml. prontosil rubrum were injected through the drainage tube. The stitches closing the external os were removed. The intracervical-uterine plug was removed. For photographs and description of the specimen see Figs. 2, 3 and 4.

On regaining consciousness after the anaesthetic the patient vomited "coffee grounds". A duodenal tube was immediately inserted; 1 pint was withdrawn. Continuous gastric suction apparatus was connected. The patient made a steady recovery.

Further bacteriological report:

Blood agar. Very light growth; scanty staphylococcus albus; viridans colonies of gram-positive cocci; scanty coliform bacilli.

Egg meat. Scanty long-chained streptococci only.

Milk under oil. Numerous long-chained streptococci. No gram-positive bacilli after 24 hours.

Serum broth. Gram-positive bacilli (? diphtheroids); gram-positive diplococci, some in chains.

No gas gangrene organisms isolated after 3 days. Viridans streptococci from milk and egg meat subcultures (aerobically).

After a total of 640,000 units penicillin and 17 grams sulfadiazine on July 18th, 1946, the patient's drug treatment ceased. Her wound healed by first intention. She was allowed up on July 24th after a vaginal examination which revealed an anteverted mobile uterus which corresponded in size to a normal uterus at this stage of involution. As the

patient would no longer stay in hospital a hysterogram was done on July 31st.

September 13th, 1946. She stated that she felt perfectly fit. She bled slightly after the lipiodol injection of July 31st, but not since.

On examination. Scar, well healed; *per vaginam,* cervix normal; uterus, could not be clearly defined.

Hysterogram done (see Fig. 5).

There was slight vaginal bleeding at the completion of the examination.

Discussion.

From the history, clinical examination, photographs and legends, the following deductions may logically be made:

1. *Angular Pregnancy.*

Figs. 2, 3 and 4 show that the Fallopian tube, round ligament and ovary are attached high up on the right side of the specimen whereas the uterine attachment of the left adnexa is below the level of the head of the foetus, i.e., the left side of the uterus did not take any active part in this pregnancy.

Therefore, the ovum was implanted either in the right cornu of the uterus, in a diverticulum, in a rudimentary horn, in one cornu of a uterus bicornis, or in a sacculus.

Against a pregnancy in a diverticulum (Bennett, 1937; DeLee, 1940c; Hawkins, 1945; Stander, 1941c) rudimentary horn (Kerr, 1944a) or uterus bicornis (Corbet, 1945) is the fact that the uterus is not separate and distinct from the pregnancy.

Sacculation (DeLee, 1940a; Stander, 1941a) can be ruled out as there is no history of pain or urinary disturbances pointing toward a displaced uterus unable to correct itself.

The situation also is against sacculation as the latter tends to affect the anterior wall in retroflexions and the posterior wall following ventral suspensions (Stander, 1941b).

The pregnancy was completely within the uterus with the placenta attached to the area over the entry of the right Fallopian tube into the uterus. It thus conforms to angular pregnancy as described by Munro Kerr (1944b) and DeLee (1940b).

2. *Constriction Ring.*

Viewing Fig. 4 will show that:

(*a*) Clinically the os was found to be 2 fingers dilated. There was a narrow cylindrical uterine channel extending from the cervix (? plus lower part of the body of the uterus—as it easily admitted a swab—*vide* "operation") to the head of the foetus.

(*b*) Operatively the foetus was found to lie in what logically was a thinned-out cornu and fundus of the uterus.

The dilated os shows that the cervix took part in the labour. That this channel was not the original uterus below the angular pregnancy is borne out by the following facts:

(i) The cervix took an active part in the labour—a function not performed with ectopic pregnancy.

(ii) Had this channel been the original uterus it should have admitted more than one finger as the uterus enlarged, due to hormonal influence, no matter where the pregnancy is situated.

Therefore it can be assumed that this ring-like channel was due to a segment of uterine muscle in spasm, i.e., a constriction ring, the site of the ring being at the junction of the affected cornu plus fundus with the body of the uterus.

The situation, embryologically, tends to favour Rudolph's (1935) theory on the aetiology of constriction ring, that is, at sites of physiological constrictions found in lower animals.

3. *Physometria.*

Both clinically—the uterus being resonant to percussion and because of the escape

of gas from the uterus when the foetal head was pushed up—and radiologically (Fig. 1) the diagnosis of physometria was established.

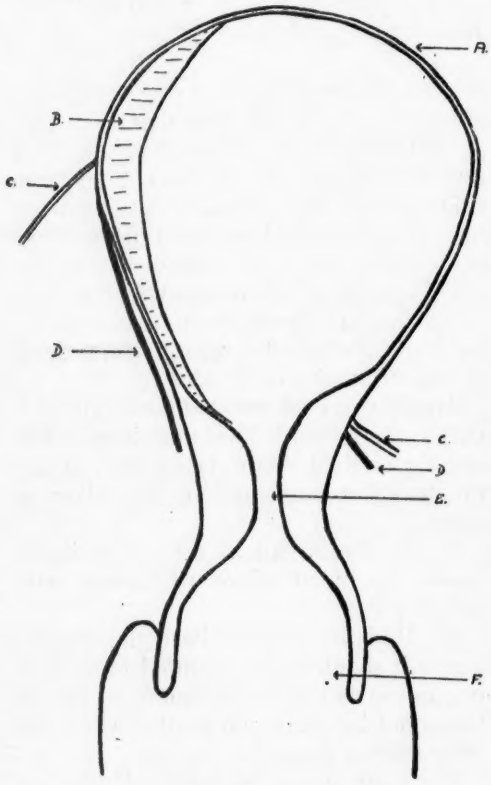

FIG. 4

Sketch of combined operative and clinical picture.

A. Thinned wall of the uterus.
B. Placenta.
C. Fallopian tube.
D. Round ligament.
E. Narrow lumen surrounded by thick uterine muscle.
F. Cervix—2 fingers dilated.

4. *Partial Destruction.*

This can be seen by studying Figs. 2 and 3. The following argument explains the course of the partial destruction.

The history suggests death of the foetus before the onset of the poor type of labour, that is, complete absence of foetal movement. The membranes ruptured early in labour.

At the onset of, or during, labour the constriction ring developed. (Vaginal bleeding occurred 4 days after the onset of abdominal cramps. Fig. 3 shows the placenta extending on to the ring. This suggests that the placenta acted "praevia" after the formation of the cervix-like ring.)

The amniotic cavity became infected, the foetus macerated. Foetal scalp sloughed, plugged the constriction ring, and prevented the escape of both infected fluid and gas. The tension within the pregnant sac increased.

According to Morison and Saint (1935) an increase in tension diminishes or cuts off the blood supply to the affected part. This in turn leads to partial destruction. Hence the gangrenous macroscopic appearance of the muscle surrounding the foetus (Fig. 2). This was confirmed histologically.

5. *Recovery.*

The patient's recovery is a remarkable feat. Her resistance, penicillin, sulpha drugs, adequate fluid balance, blood transfusions and nursing can be claimed as the responsible factors.

6. *Lipiodol in Pelvic Veins.*

In order to prove beyond doubt that the major part of the body of the uterus was still left a hysterogram was done 20 days after her operation. It was done so soon post-operatively for fear of losing sight of the patient as she threatened to sign "the red ticket and quit hospital."

The uterine cavity was poorly outlined. Lipiodol intravasation occurred into the pelvic veins. Six weeks later she returned to the out-patient department. Lipiodol again was gently injected through the cervix. Fig. 5 shows the result, again it

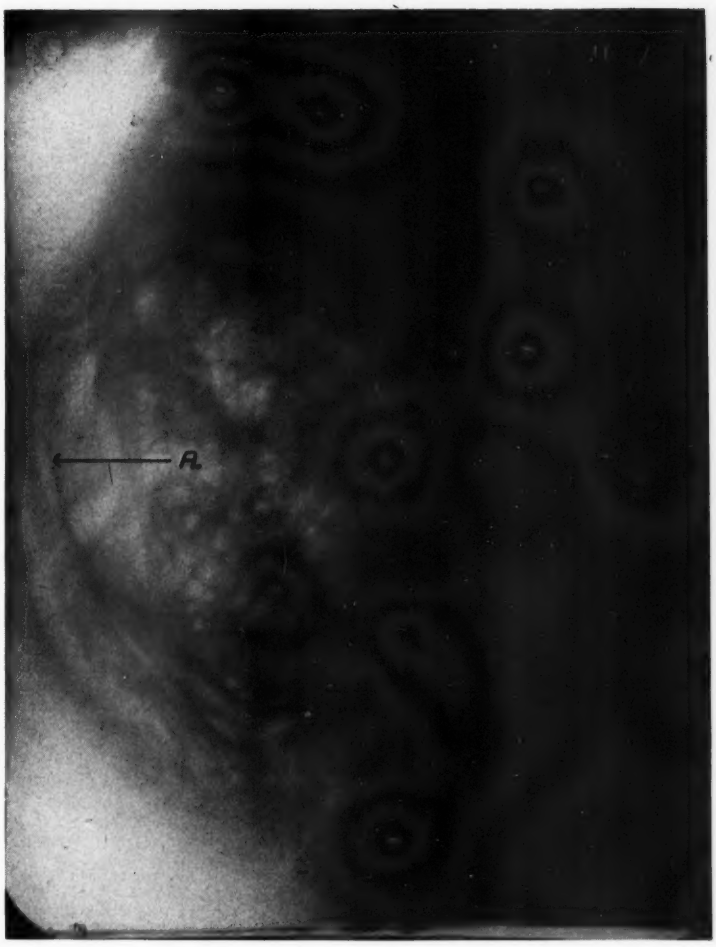

FIG. 1

Lateral view of abdomen (Portable).

A. Gas between foetus and uterus wall.

J. T. L.

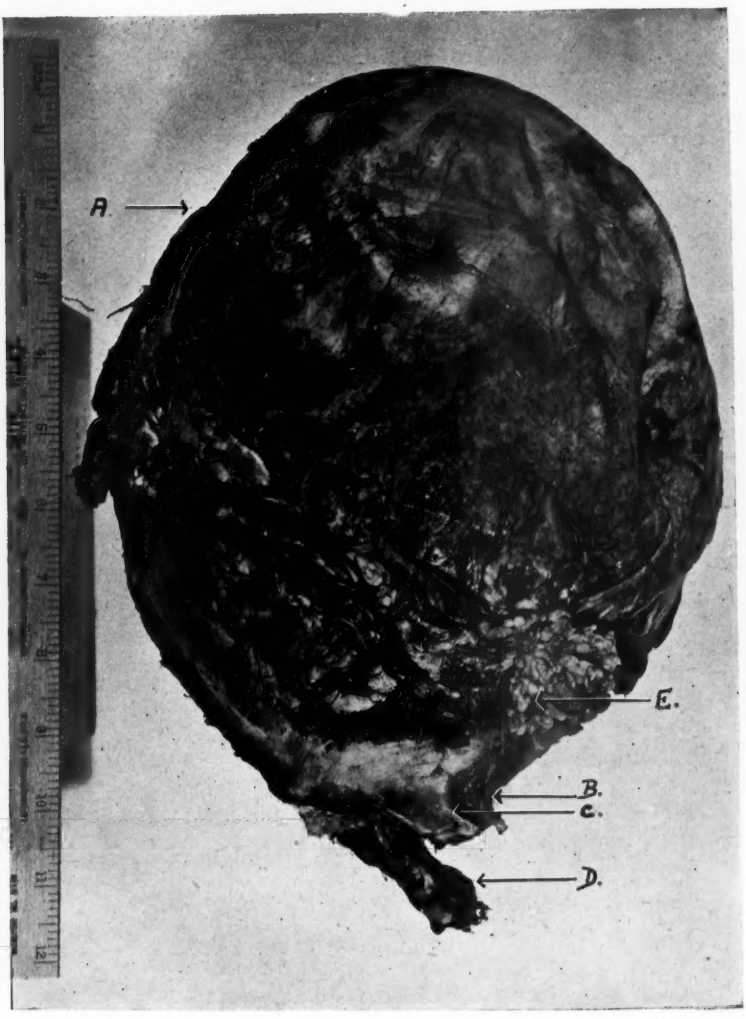

FIG. 2

Anterior view of specimen.

A. Insertion of right Fallopian tube. B. Left Fallopian tube.
C. Left round ligament. D. Scalp protruding.
E. Omental adhesion.

J. T. L.

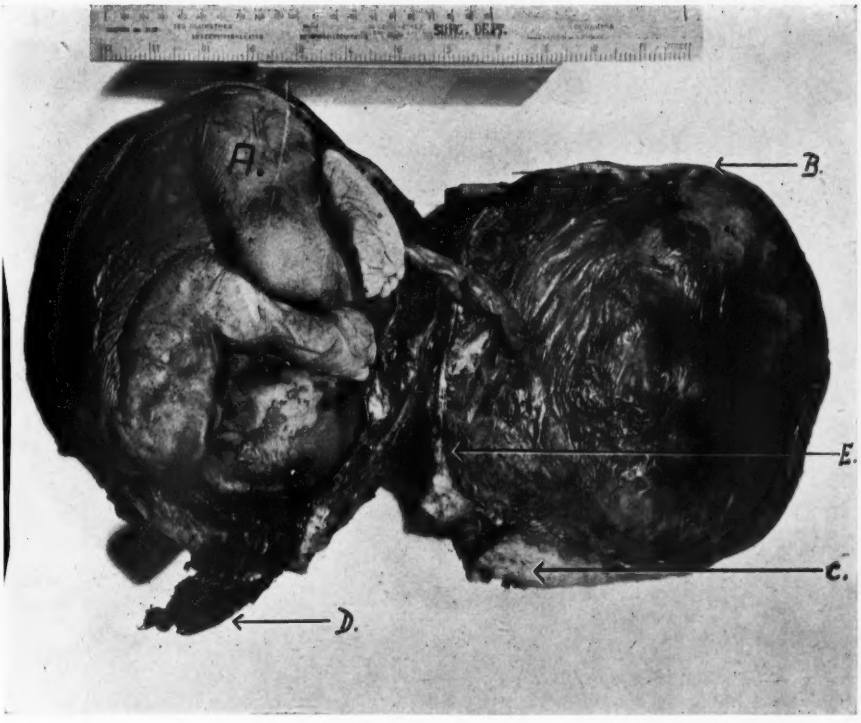

FIG. 3

Specimen opened.

A. Macerated foetus. B. Thin walled " uterus ".
C. Thick " ring " locking in the foetus.
D. Scalp protruding through the ring.
E. Placenta attached down on the thick rim (on the left side).

J. T. L.

FIG. 5

Lipiodol leaked from the uterine cavity into the pelvic venous plexus markedly on the right side.

J. T. L.

escaped into the pelvic veins. The veinous intravasation of lipiodol is a rare phenomenon (Bloomfield, 1946; Roblee and Moore, 1945). The patient has failed to report for further examination.

ACKNOWLEDGMENTS.

I wish to thank Professor Crichton and Dr. Ruby Sharp for the interest they showed in the case; Dr. Jack Smith for the skilled anaesthetic administration to this dangerously sick patient; the house-surgeons, Drs. Chait and Ahrenson; Sister Joubert and staff for the exceptional care exercised in nursing the patient; Messrs. MacManus and Taylor for their help with the photography and preparation of the slides.

REFERENCES.

Bennett, R. J. (1937): *Ann. Surg.*, **106**, 301.

Bloomfield, A. (1946): *J. Obstet. Gynaec.*, **53**, 345.

Corbet, R. M. (1945): *Brit. med. J.*, **2**, 894.

DeLee, J. B. (1940a): *Principles and practice of obstetrics*, p. 465. Philadelphia.

DeLee, J. B. (1940b): *Principles and practice of obstetrics*, p. 447. Philadelphia.

DeLee, J. B. (1940c): *Principles and practice of obstetrics*, p. 596. Philadelphia.

Gibberd, G. P. (1938): *Textbook of midwifery*, p. 596. London.

Hawkins, M. C. (1945): *Amer. J. Obstet. Gynec.*, **50**, 562.

Kerr, J. M. M., *et al.* (1944a): *Combined textbook of obstetrics and gynaecology*, p. 359. Edinburgh.

Kerr, J. M. M., *et al.* (1944b): *Combined textbook of obstetrics and gynaecology*, p. 361. Edinburgh.

Morison, J. R. and Saint, C. F. M. (1935): *An introduction to surgery*. Bristol.

Roblee, M. A., and Moore, S. (1945): *Sth. med. J.*, **38**, 89.

Rudolph, L. (1935): *J. Obstet. Gynaec.*, **42**, 992.

Stander, H. J. (1941a): *Williams' Obstetrics*, 8th edition, p. 715. New York.

Stander, H. J. (1941b): *Williams' Obstetrics*, 8th edition, p. 979. New York.

Stander, H. J. (1941c): *Williams' Obstetrics*, 8th edition, p. 714. New York.

The Effect of Methyl-Ergometrine on the Human Puerperal Uterus

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THE isolation of ergometrine in 1935 provided a drug which rapidly superseded ergotamine and ergotoxine in obstetric practice, and became recognized as being the oxytocic drug of choice during the post-partum period. Its advantages were greater potency, more rapid action, and absence of undesirable side-effects, in particular gangrene of the extremities.

The use of ergot preparations is generally considered to be contra-indicated before the end of the third stage of labour, because of the prolonged nature of the uterine response produced, but some workers, particularly in the United States and in continental Europe, have recently recommended the wider use of ergometrine. In particular, several authors (O'Connor, 1944; McConnell and Schauffler, 1943) have reported very favourably on the practice of giving the drug intravenously as the anterior shoulder appears under the pubic arch. It has also been used in uterine inertia and to induce labour, but these indications are not regarded with favour in this country because of the danger of foetal asphyxia. As an emergency measure, its administration is recommended by many obstetricians (Flew *et al.*, 1947; Moir, 1944a) for haemorrhage, associated with a relaxed uterus, occurring during the third stage of labour.

For a drug to supersede ergometrine it must at least equal that alkaloid in the qualities described, and should possess some further advantage. In 1943 Stoll and Hoffman introduced methyl-ergometrine, at first known as ME 277, and later given the commercial name of "Methergine". This substance was claimed to have all the virtues of ergometrine, to be equally free from unpleasant side-effects and to be rather more powerful.

Chemistry.

Chemically, the drug is *d*-lysergic acid butanol 2-amide tartarate. From the manufacturing point of view it has considerable advantages over ergometrine.

The yield of pure ergometrine from crude ergot is very small indeed and varies considerably from one sample to another; it is economical to extract only the better grades of ergot, and these must be imported, mainly from Spain. All the alkaloids of ergot contain in their molecular structure a complex organic acid, *d*-lysergic acid, which is itself pharmacologically inert. In any sample of ergot there are a large number of alkaloids, most of which are, however, pharmacologically inert or of little clinical value. In the preparation of methyl-ergometrine this mixture of alkaloids is broken down; the *d*-lysergic acid is extracted, and from it methyl-ergometrine is synthesized. By this means the total yield of methyl-ergometrine is of the order of eight times that of ergometrine and, as it is apparently more potent, the effective yield is greater still. Furthermore, the cruder samples of ergot may be utilized.

Pharmacology.

During the recent war methyl-ergometrine was manufactured and marketed in Switzerland and in the United States, but it has only recently become available in Great Britain. A number of reports have already been published dealing with its pharmacology and some aspects of its clinical application. Kirchof *et al* (1944) have demonstrated that it exerts a powerful oxytocic effect in the rabbit and guinea-pig. They found no evidence of toxicity in humans. They concluded that the oxytocic effect was at least equal to that of ergometrine. Bachbauer (1944) investigated tokometrically the effect on human uterine contractions during pregnancy, labour and the puerperium, and considered that its properties were similar to those of ergometrine. The drug appears to be free from the sympathicolytic effects of ergotamine and ergotoxine.

Clinical Reports.

Brougher (1945) administered the drug in doses of 0.2 mg. to 288 women as the foetal shoulder was born, and compared his results with a control series of patients to whom ergometrine was given in a similar way. The blood loss was about equal. In 3 patients manual removal of the placenta was necessary because of a contraction ring, which he attributed to delay in entering the vein whilst giving the injection. A uterine contraction occurred 20 to 30 seconds after intravenous administration, and this contraction was maintained longer in the methyl-ergometrine series.

Tollefson (1944) gave doses of 0.2 mg. to 200 patients as soon as the placenta was thought to have separated. A uterine contraction followed on an average in 48 seconds and the placenta was then expressed; there was little blood loss, but he noted an increase in after pains. In 12 cases, however, it was given before the placenta had fully separated, and the resultant contraction lasted 1 to 2 hours. Cartwright and Rogers (1946), Roberts (1944), Tritsch and Schneider (1945), Janke (1942), and d'Ernst (1946) have similarly reported that they have found it to be a highly efficient oxytocic during and after the third stage of labour.

The drug has also been given orally in dilute solution under the name of *Partergin*, and this has been used by Farber (1946) with success in the induction of labour, whilst Brunner (1946) has reported favourably on its effect in uterine inertia. However, the use of an oxytocic drug derived from ergot is potentially dangerous to the foetus as, if even moderate doses are given, there is a prolonged tense contraction of the uterus which is liable to lead to foetal asphyxia. In these experiments only very small doses were used, but even so it seems unlikely that such methods will be popular in this country. Moir (personal communication) recalls 2 cases in which ergometrine was used and an unexplained foetal death occurred. He believes that the deaths were due to foetal asphyxia associated with a degree of tonic contraction of the uterus.

The Present Investigation.

From the results of the work already published there seems little doubt that methyl-ergometrine is, from a clinical point of view, an efficient oxytocic drug and that it is apparently free from toxic effects. But a satisfactory comparison of the effects of ergometrine and methyl-ergometrine on the human uterus has not yet been published. The present investigation was undertaken in an attempt to provide such a comparison.

The technique using an intrauterine bag was adopted, the details of which have already been fully described (Moir, 1944b). In all some 24 tracings were made during the investigation.

As a standard for comparison, a series of tracings were made of the effect of the intravenous injection of 0.1 mg. of ergometrine in normal patients between the 6th and 8th days after delivery. The drug given was ergometrine maleate, but the dosage was calculated as 0.1 mg. of ergometrine alkaloid. Two typical tracings are shown in Fig. 1(a) and (b).

curve gradually returns to the original level in about 50 to 55 minutes, after which a series of rhythmical contractions follow at gradually lengthening intervals. These slowly merge into the normal puerperal waves, but last for several hours.

Methyl-ergometrine was then given to a similar series of patients. The dosages employed were all calculated as methyl-

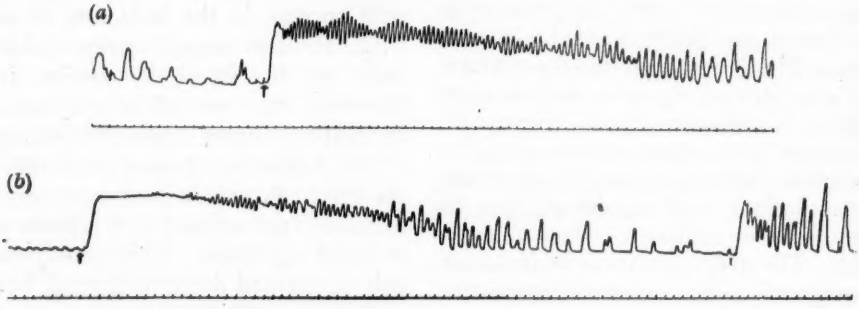

FIG. 1.

Intravenous injections of 0.1 mg. of ergometrine at ↑. In (*b*) this dose was repeated after an interval of 1 hour 15 minutes, the second response being quite different from the first.

The time markings are minutes.

The effect of an intravenous injection of ergometrine on the 6th to 8th day of the puerperium has been fully described by Dudley and Moir (1935). The tracings in the present series confirm their findings.

Prior to the injection, the uterus may or may not show rhythmical contractions, generally of low amplitude. Following the injection there is a delay of rather less than a minute followed by a sharp, strong contraction. The delay in this series averaged 55 seconds and varied between 35 seconds and 78 seconds. This is slightly longer than is usually reported (Moir, 1936).

Following the initial rise, the uterus usually remains firmly contracted for a few minutes (this period varies from about 1 to 5 minutes) and then partially relaxes, the plateau giving way to a series of small contractions which increase in amplitude. The

ergometrine-tartarate, as the preparation was received in ampoules containing 0.2 mg. of this salf. Calculated on the basis of molecular concentration, a dosage of 0.145 mg. of methyl-ergometrine-tartarate is equivalent to a dosage of 0.1 mg. of ergometrine alkaloid. A dosage of 0.1 mg. was found to be a satisfactory dose for purposes of comparison. A series of tracings were made following the intravenous injection of this dose, 2 typical examples of such tracings being shown in Fig. 2(a) and (b). Tracings were also made following smaller doses (Fig. 3) showing the effect of a dosage in molecular concentration equivalent to 0.05 mg. of ergometrine alkaloid. In addition, tracings were taken following the administration of the drug intramuscularly (Fig. 4) and by mouth (Fig. 5). Finally, the drug was

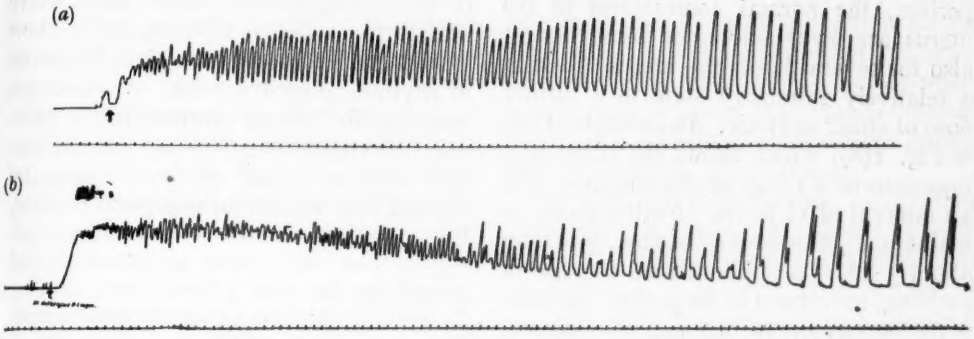

FIG. 2.

Intravenous injection of 0.1 mg. of methyl-ergometrine-tartrate at ↑.

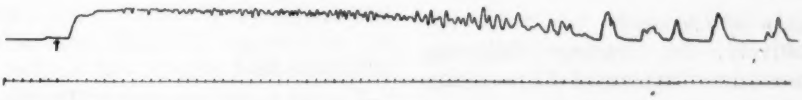

FIG. 3.

Intravenous injection of 0.072 mg. of methyl-ergometrine-tartarate at ↑.

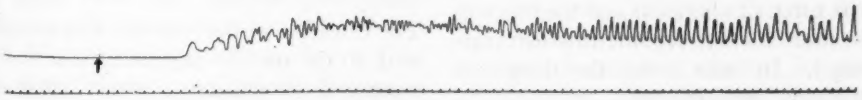

FIG. 4.

Intramuscular injection of 0.1 mg. of methyl-ergometrine-tartrate at ↑. Delay of 9½ minutes.

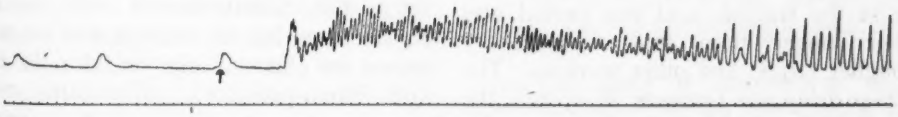

FIG. 5.

Methyl-ergometrine-tartarate 0.2 mg. was given by mouth at ↑. Delay of 7 minutes.

used clinically in a very small series of patients; 0.2 mg. of methyl-ergometrine-tartarate was given intravenously shortly after delivery of the placenta, whilst the uterus was relaxed. The delay before a firm uterine contraction could be palpated was noted; such a measurement is, of course, merely an impression and is not absolutely accurate and, furthermore, it is impossible to be certain whether the contraction felt is due to the effect of the drug or is spontaneous.

Unfortunately, it is not practicable to compare the effect of the two drugs on the same uterus on the same day. After an injection of either drug during the puer-

perium, the normal contractions of the uterus are hyperactive for some hours; also for several hours the uterus is left in a relatively refractory state to a further dose of either oxytocic. An example of this is Fig. 1(b), which shows the effect of 2 injections of 0.1 mg. of ergometrine, with an interval of 1¼ hours. Furthermore, to maintain a continuous record for more than about 3 hours is impracticable because of suckling, movement of the patient, the state of the bladder and rectum and other factors. However, the findings over a series of tracings proved sufficiently constant for an accurate comparison to be made.

Comparison of Tracings.

Qualitatively, the tracings following intravenous administration of the two drugs are very similar. Quantitatively, however, there are definite differences, and a comparison was made between the ergometrine series (0.1 mg. of alkaloid) and the tracings taken after methyl-ergometrine-tartarate (0.1 mg.). In both series the drug was administered intravenously.

The Time of Onset.

After methyl-ergometrine there was an appreciably longer delay before the initial rise in the tracing, and this period was rather longer than that reported by Brougher (1945) and other workers. The average delay was 1 minute 36 seconds, the longest period being 2 minutes 20 seconds and the shortest 50 seconds. As mentioned earlier, the average delay following ergometrine was 55 seconds. Thus it would appear that ergometrine acts more rapidly, the difference being of the order of 40 seconds.

Nature of Contractions.

The type and sequence of contractions were identical in the two series. As with the previous drug, following the injection of methyl-ergometrine, there was a sharp initial rise, usually followed by a short plateau, which in turn gave place to a series of rhythmical contractions. At about the time that the tracing returned to the base-line, the contractions became intermittent and over a period of hours gradually merged into the normal puerperal rhythm. Fig. 2(b) shows the effect of methyl-ergometrine for 1 hour 45 minutes; and recordings for over 2 hours were similar. In general, the amplitude of the contractions was considerably greater after methyl-ergometrine, though individual variations were considerable. The frequency of the contractions was much the same for the two drugs.

The Base-line

The rise in the base-line represents uterine tonus and this can be measured accurately. There was a slightly greater rise after methyl-ergometrine, the ratio being 5:4. The duration of the rise was also measured and, in the methyl-ergometrine series, this averaged 72 minutes, whilst after ergometrine it averaged 54 minutes.

Side Effects.

In no case was any toxic effect noted after the administration of methyl-ergometrine, but no attempt was made to record the effect, if any, on the pulse-rate and blood-pressure. After-pains were reproduced in all patients who had already suffered from them early in the puerperium, and in one other case. They were transient and not severe. In 3 cases retained membranes were expelled.

Intramuscular Injection.

Methyl-ergometrine was administered by this route in 2 cases and the response was disappointing. The onset of the contractions was a gradual one, commencing 7 to 10 minutes after the injection. The estab-

lished contractions and the uterine tonus were less marked than when it was given by mouth or intravenous injection. D'Ernst (1946) noted clinically that the response following intramuscular injection was unreliable. It would be necessary, however, to conduct a larger series of experiments before definitely stating that the response is consistently poor following intramuscular injection.

Oral Administration.

The drug was given orally in 1 case (Fig. 5). There was a delay of 7 minutes, after which, excepting for a less dramatic onset, the tracing was similar to those which followed intravenous injection. This is very similar to the effect of ergometrine by mouth, which has already been described by Moir (1936).

Use Immediately after Labour.

A few cases were observed in which methyl-ergometrine was given immediately after labour and the effect observed by palpating the uterus. On each occasion a firm uterine contraction was apparent within 70 seconds, usually in about 45 seconds. This agrees with the findings of Janke (1942) and Tollefson (1944). This latent period was shorter than that previously observed in the tracings (6th to 8th day of the puerperium), but a more extensive trial would be necessary to determine whether this difference in the speed of action between the very early and later puerperium is a constant feature of the drug.

Discussion.

From a comparison of these tracings, there is no doubt that methyl-ergometrine exerts a powerful oxytocic effect on the human uterus on the 6th to 8th day of the puerperium. This effect is rapid in onset, averaging 96 seconds after intravenous injection; this is 40 to 50 seconds longer than after a similar injection of ergometrine. This latent period in the puerperal uterus is longer than that previously reported as a result of clinical trials during and immediately after labour.

The effect is a powerful one, being rather more than 1.5 times as strong as with ergometrine when doses of equal molecular strength are compared. Thus, a dose of 0.2 mg. of methyl-ergometrine-tartarate is roughly equal in effect to a dose of 0.25 mg. of ergometrine alkaloid. The duration of the contractions is rather longer, the ratio being of the order of 4:3. Qualitatively, the drugs are almost identical. Methyl-ergometrine appears to be free from toxic effects. Theoretically the extra delay is a slight disadvantage, at least in cases of severe haemorrhage, but the blood loss in 40 seconds would not be very great and may to some extent be offset by the more prolonged oxytocic effect. This appears to be the only point in which it is inferior to ergometrine. Certainly the drug is worthy of an extensive clinical trial.

Summary.

1. Methyl-ergometrine ("Methergine"), a new semi-synthetic ergot alkaloid, is described.

2. The effect of ergometrine and of methyl-ergometrine on the human puerperal uterus is compared.

3. Methyl-ergometrine is a powerful oxytocic drug, free from undesirable side-effects, with properties which closely resemble those of ergometrine.

4. As an oxytocic, methyl-ergometrine is, weight for weight, between 1.5 times and twice as powerful as ergometrine.

5. When methyl-ergometrine is administered intravenously, on the 6th to 8th day of the puerperium, the delay before the

uterus contracts is slightly greater than with ergometrine.

6. Weight for weight, methyl-ergometrine exerts a slightly more prolonged effect on the uterus than does ergometrine.

7. Methyl-ergometrine is effective when given by intravenous injection or by mouth; but the onset appears to be slower, and the contractions are less marked, if it is administered by the intramuscular route.

ACKNOWLEDGEMENTS.

The writer carried out this work in the Nuffield Department of Obstetrics and Gynaecology, Oxford, whilst holding a Walter and Eliza Hall Travelling Medical Research Fellowship of the University of Sydney. I express my thanks to Professor J. Chassar Moir for his constant advice and encouragement and for the loan of the apparatus which he devised, and I am grateful to the nursing staff and patients for their willing co-operation.

The Methergine was supplied by Sandoz Products Ltd., London.

REFERENCES.

Bachbauer, A. (1944): *Geb. u. Frauenklin.*, **6** 278.

Brougher, J. C. (1945): *West. J. Surg.*, **53**, 276.

Brunner, C. (1946): *Gynaecologia*, **122**, 114.

Cartwright, E. M., and Rogers, W. C. (1946): *West. J. Surg.*, **54**, 59.

Dudley, H. W., and Moir, J. C. (1935): *Brit. med. J.*, **1**, 520.

d'Ernst, J. P. (1946): *Schweiz. med. Wschr.*, **76**, 775.

Farber, E. P. (1946): *Amer. J. Obstet. Gynec.*, **51**, 859.

Flew, J. D. S., *et al* (1947): *Proc. R. Soc. Med.* (In press.)

Janke, G. (1942): *Zbl. f. Gynäk.*, **66**, 1071.

Kirchof, A. C., Racely, C. A., Wilson, W. M., and David, N. A. (1944): *West. J. Surg.*, **52**, 197.

McConnell, G., and Schauffler, G. C. (1943): *West. J. Surg.*, **51**, 403.

Moir, J. C. (1936): *Brit. med. J.*, **2**, 799.

Moir, J. C. (1944a): *J. Obstet. Gynaec. Brit. Emp.*, **51**, 247.

Moir, J. C. (1944b): *J. Obstet. Gynaec. Brit. Emp.*, **51**, 181.

O'Connor, C. T. (1944): *Amer. J. Obstet. Gynec.*, **48**, 683.

Roberts, P. C. (1944): *West. J. Surg.*, **52**, 380.

Stoll, A., and Hoffman, A. (1943): *Helvet. Ohim. Acta*, **26**, 944.

Tollefson, D. G. (1944): *West. J. Surg.*, **52**, 383.

Tritsch, J. E., and Schneider, E. (1945): *Amer. J. Obstet. Gynec.*, **50**, 434.

The Antenatal and Postnatal Care of the Erythroblastotic Infant*

BY

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THE problem of the erythroblastotic infant is one which, although not of everyday occurrence, is met with sufficiently often to warrant the adoption of a proper scheme of treatment. Such a scheme should be based on the underlying scientific principles involved in the aetiology of the condition. The incidence of erythroblastosis is approximately 1 in 300 of all pregnancies (Haldane, 1942; Whitby and Britton, 1946a): for comparison it is rather more common than face presentation, which occurs about 1 in every 300 labours. The number actually treated in obstetric centres will be greater than this because of those referred from domiciliary cases and nursing homes as being in need of special treatment. The state of many such infants, upon their arrival in hospital, makes it obvious that adequate treatment is, as yet, available only in a few specialized centres. When it is remembered that the mortality of untreated cases of erythroblastosis foetalis ranges from 50 to 80 per cent and that as high as 10 per cent of the cases which recover may be affected by central nervous system lesions (Hawksley and Lightwood, 1934; McKinley, 1941) or hepatosplenomegaly (Drummond and Watkins, 1946), it is highly desirable that such cases should be anticipated whenever possible, so that adequate treatment is available when required.

An extensive literature has already accumulated on the subject of erythroblastosis. This year there have been more than 90 publications on the subject to date, ranging geographically from Iceland to New Zealand, and in subject matter from complex genetic theories, such as that expounded by Fisher and Race (1946), to simple case reports (Venters, 1946). As yet however, there has been no attempt to apply the genetical and serological evidence to the formation of a practical guide for the treatment of affected cases. This paper is an attempt to fill this gap, until such time as a more comprehensive knowledge of the subject will dictate a more complete method of management.

It is based not only on the study of almost a score of cases occurring in the Jessop Hospital for Women during the last 12 months, each of which was as fully investigated as our knowledge at that time allowed, but also on an extensive use of the records of the National Blood Transfusion Service Sheffield Regional Laboratory, with whom we work in close co-operation.

THE ANTENATAL CARE.

In the first place erythroblastosis should be "anticipated". The word "anticipated" is used advisedly, as infants who will be affected can generally be detected before birth. A note of the routine procedure to discover these cases is given here.

All women at their first visit to the antenatal clinic should have blood taken for blood grouping, rhesus typing and a serological test for syphilis. If found to be Rh positive, as 85 per cent of women are, further investigation need not be made. If the woman is Rh negative and primigravid, further steps need not be taken

* A paper read to the North of England Obstetrical and Gynaecological Society—November 1st, 1946.

until the the eighth month. At the Sheffield Regional Transfusion Service Laboratory over 1,000 Rh negative primiparae had this first blood specimen tested for atypical agglutinins, with completely negative results. Because of this, tests for atypical agglutinins have been discontinued at this stage. At the eighth month, however, the blood should be again examined to confirm the Rh typing, and tested for atypical agglutinins in the serum. In most cases the result will again be negative, although a French paper (Hoet, de Somer and Vandenbroucke, 1946) reports an investigation into 60 families with erythroblastotic babies in which antibodies were found in the mother's serum in 8 cases of icterus in first-born children. These figures are so at variance with the findings of other workers, however, that they should be treated with great reserve.

In Rh negative multiparae, without a history suggestive of previous trouble, atypical agglutinins should be searched for at least once before the eighth month of pregnancy. It must also be remembered that a previous transfusion may have produced the same effect as a "sensitizing pregnancy", and this must be borne in mind until we know that there are no hospitals where a female child or woman of child-bearing age, is transfused before the rhesus typing has been determined. In an emergency Rh negative blood should be used. Once atypical agglutinins are discovered their titre should be determined and re-determined each month until delivery.

Even more care should be exercised in the supervision of multiparae with a definite history of children affected by erythroblastosis foetalis. The serum should be tested for agglutinins monthly throughout pregnancy, even though such tests may give negative results. On each occasion the tests should include not only those for the complete agglutinins, but also the Coombs' test (Coombs, Mourant and Race, 1945) for the incomplete or "blocking" antibody. This may sound like a great deal of investigation but it is not suggested without reason.

There is little doubt now that premature interruption of pregnancy is of value in properly selected cases. The foetus is removed from its harmful environment before the mother's antibodies have had time to complete the damage which they cause. However, following a careful study of all the case records available, one cannot but agree with the statement by Whitby and Britton (1946b), that "the titre of the anti-Rh antibodies in the mother is no criterion of the severity of the disease in the foetus." Nevertheless, this may be an apparent finding and not a truly accurate one. The number of such cases published, where the behaviour of the titre of the antibodies during the whole pregnancy is known, are very few. The statement that "the titre of the anti-Rh antibodies in the mother just before term is no criterion of the severity of the disease in the foetus" may be more accurate. Because of this the routine monthly testing of known or suspicious cases is advocated, for only when a large series of serological findings is finally correlated with the clinical results can a final verdict be passed.

An example of the apparently anomalous results so far obtained, but one which may fit into the scheme when a sufficient number of cases have been properly investigated, is quoted below:

Mrs. O., 3rd gravida.

First pregnancy in 1940, a mature female child weighing 7 pounds 3 ounces was born alive by natural forces. There was a history of jaundice shortly after birth, but the child is now alive and well.

Second pregnancy in 1944, a premature male

infant weighing 6 pounds 15 ounces was born at the 36th week. Delivery was normal. The infant died deeply jaundiced on the 5th day.

The husband was then found to be Rh positive —homozygous.

Third pregnancy—confinement due June 13th, 1946. At the seventh week her serum showed "Anti-Rh present in moderate strength". At the 11th and 15th weeks "atypical agglutinin, presumably anti-Rh, still demonstrable at a very weak titre" was reported. At the 19th, 23rd and 28th weeks "no atypical agglutinin demonstrable at room or incubator temperature, and no incomplete antibody by the Weiner technique" was reported.

Three days after the last test a stillborn hydropic infant was delivered at 28 weeks, and 8 days later anti-Rh was demonstrable in the form of the incomplete anti-D variety.

This is perhaps an extreme example of the point I wish to make. Had this patient not been tested from her first appearance it would have been said that her serum gave no indication of trouble, because the presence of anti-Rh so early in the pregnancy would have been missed.

Method of Delivery.

When complete records of a larger series of cases are available, fluctuations in the titre of the maternal antibodies may afford an indication of the severity of the disease in the foetus, and even dictate when to interfere; but at the moment, in the absence of such guidance, there is no doubt that the decision to perform Caesarean section or induction of labour must be made on the history. There are only two exceptions to this working rule which I can call to mind. Firstly, in the case where, on the history, trouble is considered inevitable, and yet, from the beginning of the pregnancy the routine serum tests all give negative results. Here the husband must be genotyped, as it is possible that he may be heterozygous. His wife may have carried 2 or 3 Rh positive children, but this particular one may be Rh negative and therefore unaffected. Obviously interference in such a case is completely unwarranted. In this respect it has been proved that there is a preponderance of homozygous fathers (Taylor and Race, 1944). I have been unable to find any case reported of an Rh negative woman, who has previously been sensitized to Rh positive antigen, carrying another Rh positive child without producing further antibodies.

Secondly, before performing Caesarean section, the foetus must always be X-rayed, not only to exclude the usual foetal abnormalities, but on rare occasions hydrops may be detected—the so-called Javert's sign (Javert, 1942)—in which case operation is, of course, contra-indicated.

Caesarean section is usually chosen as the method of terminating the pregnancy for 3 reasons. Firstly—these infants stand the strain of labour badly; not only because of their anaemic condition, but because of their increased tendency to bleed, which will be referred to shortly. The passage of a premature head through the pelvis, in an infant with a known predisposition to haemorrhage, is not desirable. Secondly, according to Javert (1942), another of the complications of labour in these cases is premature separation of an oedematous placenta. Interesting in this connexion is the observation that in cases of accidental haemorrhage the incidence of Rh negative women is higher than the normal 15 per cent. Thirdly, of course, there are the usual risks attendant upon the induction of premature labour in any case. In spite of these points, I think that in the case of a multipara with a normal pelvis, who has a vertex presentation, and has been allowed to continue beyond the 36th week of the pregnancy, surgical induction without rupture of the membranes is sometimes indicated.

During the last week, whilst preparing this paper, a most instructive case of a nature hitherto unreported has occurred.

An Rh negative woman (Mrs. A.) had 2 children, both Rh positive, genotype R_1r, the second of which suffered from icterus gravis neonatorum. Her husband was Rh positive but heterozygous. During her third pregnancy she was kept under close observation, and at the 35th week incomplete antibody was detected for the first time. Two weeks later this was much stronger at a titre of 1 in 32. In view of the past history and the fact that the incomplete antibody is believed to be the most pathogenic one (Cappel, 1946), labour was induced at the 38th week. Blood was given to the baby through the cord after delivery. It was found subsequently that the infant was Rh negative and unaffected.

The explanation of this apparent anomaly lies almost certainly in the fact that the third pregnancy afforded a non-specific stimulus, resulting in the reappearance of atypical agglutinins originally evoked by the second foetus. This problem had not previously been encountered, and it is suggested that in cases such as these, where the father is heterozygous and atypical agglutinins appear in the maternal circulation before delivery, preparation should be made to transfuse the infant after delivery, but the decision as to whether this should be done should be delayed until its necessity is demonstrated by a simple haemoglobin and red cell count. If this is done immediately upon birth the result can be known whilst the cord vessels are still available for transfusion purposes.

Treatment of the Child.

The tendency of the erythroblastotic infant to haemorrhage has already been mentioned. Authorities differ as to the reason for this, some attributing it to a low blood prothrombin level (Dam, Tage-Hansen and Plum, 1939), and others to a deficient number of platelets (Wiener and Wexler, 1943). Whatever the reason, there is little doubt that the tendency can be favourably influenced by the administration of vitamin K. Ideally it should be given, not to the infant after delivery, but to the mother before delivery. It has even been suggested that all Rh negative blood donors should be given adequate doses of vitamin K before donating blood, so that any Rh negative blood used in the treatment of jaundiced infants would have its full prothrombin content. This paper being concerned primarily with treatment, 2 small practical points of vitamin K therapy may be mentioned. It is effective if given to the mother as little as 4 hours before delivery. If given orally, bile salts should be given at the same time to break up the fat vehicle and obtain maximum absorption. When given to the infant, preferably intramuscularly to get the most rapid effect, a water soluble preparation is recommended, since an oily solution inevitably leads to a certain number of abscesses at the injection sites, however careful the asceptic technique. Since changing to the watery solution further complications of this nature have not been encountered.

Therapy with vitamin K is not the sole prophylactic treatment for haemorrhage. All affected infants should be treated with the same respect as is shown to a breech delivery, and kept quietly in the nursery for some days. Unheralded cerebral haemorrhage on the third day has been known to occur with a normal vertex delivery from a 2nd gravida and has been subsequently confirmed postmortem.

Turning to the subject of transfusion, there is general agreement that the transfusion of compatible Rh negative blood is the most effective treatment for this condition. There has been, as yet, little attempt to say when, how and how much to give. A study of the haemoglobin percentage

and the red blood cell count of our cases by graphing the results on a logarithmic scale, coupled with examination of the blood films, has encouraged the formation of certain tentative opinions. Mention of these may serve to stimulate other investigators.

From this point one must assume that not all cases have come from one's own antenatal clinic and therefore have not been "anticipated". Indeed the question of diagnosis may arise. A discussion into the differential diagnosis of jaundice in the newborn would be out of place in this paper, but one pitfall must be avoided. If the investigator decides to be guided by the appearance of the blood film taken from the baby's circulation, and waits until such time as the textbook description of erythroblastosis is seen, in many cases he will either wait until fatal, or at any rate grievous damage has been done. Treatment must be undertaken early and confidently even where the blood film approximates to normality. It should be remembered that a certain number of normoblasts and reticulocytes will be found in the normal newborn infant's blood. Of far greater significance is the finding of jaundice coupled with any degree of anaemia—the colour index, by virtue of the fact that the red blood count is proportionately lower than the haemoglobin, being consistently high. I think some importance should be attached to the colour index as an indication of the activity of the haemolysis which is going on.

Lack of space precludes explanation of the physiological reasons for this, or description of the technique which may be necessary to obtain haemoglobin-values in the presence of jaundiced serum.

The fact remains that as a simple laboratory estimation of the severity of the disease it is of assistance. The colour index has been above 2 in one of our cases and approaching 2 in several others. As the haemolytic process exhausts itself the value falls. The infant at the same time becomes increasingly anaemic, so that a low colour index does not mean that treatment is not needed. Allowance must also be made for the effect that transfusion will have on the colour index, once treatment has been commenced.

In all cases a sample of blood from the infant should be taken for Coombs' testing, before transfusion. It is important to obtain the specimen before fresh blood is given, because the donated blood may later mask the true state of the blood of the infant (Cathie, 1946), most of which may have been haemolyzed at the time of sampling. This would make the investigation of the baby's blood difficult or impossible. A recent case at the Jessop Hospital for Women, although known to be in an Rh positive baby, by virtue of the antibodies the mother had manufactured, after two transfusions became Rh negative to all tests. One must postulate that all its own blood had been destroyed and it was, in fact thriving on donated blood. In this case the true blood group was determined from the infant's bone marrow, which is not affected by transfusion (Cathie, 1946). We are still waiting to find out when the blood stream again returns to normal. This is not entirely an academic point and has a practical application. At the beginning of this paper, I lodged a plea for more routine antenatal tests in known cases, so that antibody titres can be obtained and studied. Sometimes there are 2 different antibodies present, the titre of each varying, and not necessarily bearing any relation to that of the other. In the infant it is possible to detect the two antigens responsible for these two antibodies. During the course of treatment it

sometimes happens that one of these antigen-antibody complexes becomes undetectable—presumably the reation burns itself out more quickly than the other, which may also disappear later. It is then that the true antigen make-up of the infant's blood can still be detected in the bone marrow. It is possible that a study of antibody titres before delivery, correlated with the subsequent behaviour of the antigen-antibody reaction after delivery, will allow a more accurate forecast of the progress of the disease in other cases.

Regarding the actual technique of transfusion—Rh negative red-cell concentrate should always be used and given intravenously. Any given volume of this is equivalent approximately to twice that volume of normal blood—a great help when red cells are wanted and not fluid. The cells used should be as fresh as possible. The average life of a freshly donated and transfused erythrocyte is about 60 days, as opposed to the 120 days which is the average life of a normal red cell *in vivo* (Callender and Loutit, 1946). The present anti-coagulant in use in the blood banks of this country allows a safe store life of 21 to 28 days. If red cells which have been stored for 10 days are transfused, their life in the recipient is, however, not 50 days but slightly less. In other words, the longer the blood has been stored, the shorter the time it will remain effective after transfusion. In erythroblastosis the number of transfusions which can be given with comparative ease is limited by the number of easily accessible veins. There are seldom more than 4 of these, and it is therefore desirable that each transfusion should last for the maximum length of time. During this time the antibody will be engaged with the erythrocytes manufactured in the child's own marrow.

Taking 40 ml./pound body weight as the normal blood volume of an infant (Gimson, 1943), 150 ml. of packed red cells are equivalent to the total blood volume of an average 7½ pounds child. I can see no reason for ever giving a larger transfusion than this at one time. When one remembers that these infants are often very anaemic, with a corresponding anoxaemia of the myocardium, it is surprising that transfusion is tolerated so well.

The speed of administration is a debatable point. Presumably a slow drip, taking some 6 to 8 hours would be the ideal method. My criticism of this is that ordinary blood will seldom drip satisfactorily at this slow rate through a necessarily small bore needle. Red-cell concentrate is even more difficult to manage. Also there are few departments which can spare a pair of trained hands to hold a baby still for that length of time. Personally, I give the blood with the aid of a small two-way syringe at the rate of about 2 ml. per minute. This may seem rather rapid. The method certainly makes the operation very much easier and no untoward effects have been noted. All these infants have been followed up for months by our paediatrician, who has reported consistently good results.

Lesions of the central nervous system following erythroblastosis have already been briefly referred to. It seems probable that these lesions are due, not to the jaundice *per se*, but to a prolonged cerebral anaemia. Professor Naish, with whom I discussed this, agreed with this point of view and instanced the parallel case of the cretin. A cretin showing signs of mental deficiency within a week or two of birth will never recover with treatment as well as the case where mental signs do not become apparent until 3 or 4 months of age.

This suggests that the neurons are more sensitive to slight changes during the few

weeks following birth than later on. In support of this view the cranial nuclei of one 3 days old erythroblastotic baby, which died a few minutes after arrival at the hospital, showed deep yellow staining, but histological examination did not demonstrate any abnormality of the nervous tissue. Also infants jaundiced from other causes are not subject to such nervous sequelae. I would advance this theory as a reason for transfusion if the haemoglobin level drops below about 90 per cent in the first week, or 80 per cent later on. Levels of 50 or 60 per cent should certainly not be allowed to occur.

Finally, breast feeding must be briefly discussed. All authorities from Sheldon (1945) to Greenhill (1945) suggest, somewhat diffidently, that as antibody sometimes occurs in breast milk, breast feeding should be discouraged. The superiority of natural feeding, especially in anaemic children liable to secondary infection, need not be stressed here. Following a suggestion from Dr. Aubert of the Sheffield Transfusion Centre, that the antibody, being a protein, should surely be digested and thus rendered harmless, some experiments were undertaken. The antibody is present in the aqueous fraction of the milk and follows the same biochemical laws of digestion as do other proteins. Its presence in the aqueous fraction rules out the possibility of its being ingested after adsorption on undigested fat molecules, which are known to pass straight into the blood stream.

Clinically, the controls which have been artificially fed have certainly done no better than the breast-fed infant, and until incontrovertible evidence is available to condemn the practice, I would strongly recommend that all cases be breast-fed.

In conclusion, I would refer to the work of Haldane (1944), who pointed out that erythroblastosis foetalis is responsible for more deaths than any other inherited condition—perhaps for more than all of them put together. I feel that this alone justifies discussion of the subject.

I wish to express my thanks to the members of the Honorary Staff of the Jessop Hospital for Women for the use of their cases, to Dr. Aubert of the Sheffield Blood Transfusion Service for much helpful advice, and to Mr. Ivor Dunsford for performing the serological investigations involved.

REFERENCES.

Callender, S. T., and Loutit, J. F. (1946): *Proc. R. Soc. Med.*, **39**, 755.

Cappell, D. F. (1946): *Brit. med. J.*, **2**, 601.

Cathie, I. A. B. (1946): *Lancet*, **2**, 418.

Coombs, R. R. A., Mourant, A. E., and Race, R. R. (1945): *Brit. J. exper. Path.*, **26**, 255.

Dam, H., Tage-Hansen, E., and Plum, P. (1939): *Lancet*, **2**, 1157.

Drummond, R. J., and Watkins, A. G. (1946): *Brit. med. J.*, **1**, 984.

Fisher, R. A., and Race, R. R. (1946): *Nature, Lond.*, **157**, 48.

Gimson, J. D. (1943): *Brit. med. J.*, **2**, 293.

Greenhill, J. P. (ed.) (1945): *Yearbook of Obstetrics and Gynecology*, p. 289.

Haldane, J. B. S. (1942): *Ann. Eugen.*, **2**, 333.

Haldane, J. B. S. (1944): *Brit. med. J.*, **1**, 262.

Hawksley, J. C., and Lightwood, R. (1934): *Quart. J. Med.*, **3**, 155.

Hoet, J. F., de Somer, P., and Vandenbroucke, J. (1946): *Presse méd.*, **54**, 249.

Javert, C. T. (1942): *Surg., Gynec. Obstet.*, **74**, 1.

McKinley, H. (1941): *Arch. Dis. Childh.*, **16**, 63.

Sheldon, W. (1945): *Diseases of infancy and childhood*, London.

Taylor, G. L., and Race, R. R. (1944): *Brit. med. J.*, **1**, 288.

Venters, M. (1946): *Brit. med. J.*, **2**, 84.

Whitby, L. E. H., and Britton, C. J. C.)1946a): *Disorders of the blood*, London, p. 358.

Whitby, L. E. H., and Britton, C. J. C. (1946b): *Disorders of the blood*, London, p. 357.

Wiener, A. S., and Wexler, I. B. (1943): *Amer. J. clin. Path.*, **13**, 393.

Pregnancy after the Menopause

(A case-report and a review of the literature)

BY

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" Now Abraham and Sarah were old . . . and it had ceased to be with Sarah after the manner of women."

" For Sarah conceived and bare Abraham a son in his old age."

(Gen. xviii, 11 and xxi, 2.)

" And they had no child because that Elisabeth was barren and they both were now well stricken in years " . . . " and after those days his wife Elisabeth conceived . . . (her) full time came that she should be delivered and she brought forth a son."

(Luke, i, 7, 24 and 57.)

THAT Sarah was beyond the menopause when she conceived seems to be indisputable. Her age is alleged to have been 90, but Biblical estimates of age are perhaps more symbolic than factual. There is no indication in the story of Elisabeth as to the incidence of the menopause. The historians of the Bible refer on many occasions to pregnancies occurring at the extreme age: such occurrences were looked upon as miracles and the offspring usually were remarkable in their subsequent careers. It may be that only when the offspring showed supernormal tendencies was the fact that the mother was old considered worthy of comment. It is of course likely that the birth of a mongol would not be recorded, though it is interesting to speculate on the possibility that a mentally defective child born of abnormally aged parents might show in later life the qualities of frenzy or delusion in such a manner as to fit him for the *rôle* of prophet.

Within more recent years documented references to truly post-menopausal pregnancy are rare. There are a number of recorded cases of pregnancy occurring after surgical castration, but of the 11 which have been traced only 5 can be considered valid. In several menses had returned or had continued after the operation, and it must be assumed in every case that some ovarian tissue, normally placed or ectopic, had remained.

Pregnancy after attempted X-ray or radium castration is also reported: in some cases the castration was admittedly ineffective in that menses continued or returned, and in others it must be assumed that the more mature follicles sustained little damage. It is the possibility of such an occurrence, in which the child born may have damaged germ plasm and be sterile, or produce monsters in later life, which causes some workers to be chary of administering X-ray castration to a woman whose reproductive life is still incomplete.

The natural menopause appears to be less fraught with the risk of belated pregnancy. In all, only 15 cases have been traced in the literature, and in several of these the duration of amenorrhoea prior to

delivery was less than 2 years. A distinction must clearly be drawn between cessation of menses and the incidence of the climacteric. Oligomenorrhoea with a flow only once or twice a year, even amenorrhoea of 2 or more years duration, is not uncommonly noted in younger women. In 1 of our own sterility cases there was a history of menarche at 17 years, and subsequent menses at 20 and 25 years, with the association of headaches and flushes suggesting depressed ovarian function. A course of follicle-stimulating hormone was given 9 months after the last recorded menstrual flow and 2 monthly periods occurred, followed by a pregnancy which went to term without incident and was succeeded by regular menses.

Priou (1865) describes a woman aged 72 who had an abortion, and Boldt (1914) had a case of abortion, proved histologically, 1 year after the last menstrual period and 3 years after the onset of menopausal symptoms. Renaudin reports a pregnancy 12 years after the cessation of menses, and Kennedy (1882) had a most astounding patient who is said to have had 5 labours and 1 abortion after her fiftieth year. The duration of amenorrhoea prior to this fertile period of life is not known.

Deliveries of living infants are described by Depasse (1891) 9 years after the menopause, by Buckle (1910) 11 years after, by Underhill (1879) and Levasseur (1873) 2 years after, and by Hann (1902) 3 years after, and the latter quotes a case from Pearson whose period of amenorrhoea was 18 months. Most of the infants appear to have been normal, though that described by Brandt (1922) was an achondroplasic. Ballon (1941) reports a twin pregnancy after the menopause. Mongolism or other mental defect is not recorded in any of these children, but there appears to have been no close follow-up of the cases.

Additional case-reports come from Mayer (1908), Hirschberg (1910), Hofstätter (1922) and Numberger (1924) but the details are not available.

In none of the reported cases is there any mention of return of menses prior to conception, and it must be assumed that in each one the pregnancy followed an ovulation which had not been associated with any menstrual cycle. In the cases of Hann and Buckle menses returned for a short period after the birth, in the remainder there is no mention of subsequent menstrual function.

It is a well-established fact that some ovarian activity may continue long after the apparent menopause, even though there has been a period of flushes and headaches and other subjective symptoms. It is probable that follicular development may continue and ovulation occur at irregular intervals after a symptomatic menopause, and at laparotomy one not infrequently encounters very active looking ovaries even in old women. Nor is it especially rare to find normal external genitalia with healthy vaginal mucosa and a fair growth of Doderlein's bacilli and of glycogen-containing squames many years after the last menstrual period, which findings are strongly suggestive of continued oestrogenic activity. Resumption of menstrual activity years after the menopause has been described, and though in most cases the bleeding is "pseudo-menstrual" and associated with granulosa-cell tumour, or even carcinoma of the uterus, every surgeon must have encountered cases where no such pathology was found to account for the return of uterine bleeding, and where curettings have merely shown a normal proliferative phase.

In the case of post-menopausal pregnancy described below, it was not possible at that time to carry out hormone investiga-

tions. No previous accurate medical observations of the patient were available, but the history was typical of the menopause, and the woman had every right to assume that her days of child-bearing were over.

CASE HISTORY.

Mrs. C. T., aged 45 years, was referred to the Newcastle General Hospital on January 7th, 1944. She gave a history that her last menstrual period had been 3 years previously, preceeded by a period of scanty and less regular losses, and that she assumed that she had passed through "the change of life." The onset of menses had been at 15½ years of age. In spite of her amenorrhoea there had not, however, been any significant flushes or other menopausal symptoms. She had recently contracted scarlet fever and had been in the local isolation hospital, and during her stay there had noticed swelling of her abdomen. This had increased following her discharge from hospital after a stay of 5 weeks, and her doctor had found an abdominal tumour, apparently a pregnancy.

She was a rather stout but healthy-looking woman, grey haired and "motherly" in appearance, who looked all of her 45 years. Physical examination revealed no disease, her blood-pressure was 120/70 and there was an undoubted pregnancy of approximately 30 weeks in size, with a breech presentation. Her obstetric history included 5 previous pregnancies and was satisfactory except for the birth of premature twins, both of which had died.

She attended the antenatal clinic regularly and at 36 weeks the presentation was still a breech. External version without anaesthetic failed, and in view of her previous normal labours and the fact that her pelvis was very roomy, no attempt was made to correct the presentation under anaesthetic.

Labour commenced spontaneously on March 23rd, and the first stage was rather prolonged, though without distress. Delivery of the frank breech was assisted with forceps applied to the after-coming head, and the placenta was expelled 10 minutes later.

Her puerperium was uneventful, but lactation failed completely. She was discharged on the 14th day, and when seen at postnatal clinic 2 months later the findings were those to be expected at a postnatal examination of a multipara. There had not been any further menstrual losses and to date there is no record of return of menses or of another pregnancy. The child weighed 8 pounds 4 ounces at birth and was 21 inches in length, and appeared to be perfectly normal in every way.

It had been expected that hypertension might develop during pregnancy, but the highest recorded blood-pressure was 144/88 with no oedema. Labour was more characteristic of a primipara than a multipara, but this might be explained by the presence of a breech presentation. The only point of special interest is the complete absence of lactation, though breast feeding had been normal in all previous pregnancies.

REFERENCES.

Pregnancy after surgical castration.

Doran, A. (1902): *J. Obstet. Gynaec.*, **2**, 1.

Gordon, S. C. (1896): *Amer. J. Obstet. Gynec.*, **2**, 28, 79.

Kossman (1900): *Amer. J. Obstet. Gynec.*, **41**, 839.

Morris, M. A. (1901): *Boston med. surg. J.*, **144**, 86.

Robertson, J. A. (1890): quoted by Doran.

Schatz (1895): quoted by Doran.

Smith, L. (1902) *J. Obstet. Gynaec.*, **2**, 6.

Sutton, S. (1896): quoted by Doran.

Pregnancy after X-ray castration

Riboni, S. (1938): *Atti Soc. ital. Ostet. Ginec.*, **34**, 252.

Rosenberg, M., and Schenck, S. B. (1942): *Amer. J. Obstet. Gynec.*, **43**, 1033.

Pregnancy after natural menopause

Ballon, L. (1941): *Brit. med. J.*, **1**, 121.

Boldt (1914): *Amer. J. Obstet. Gynec.*, **69**, 345.

Brandt, M. L. (1922): *N. Y. St. med. J.*, **116**, 38.

Buckle, L. (1910): *J. Amer. med. Ass.*, **55**, 568.

Depasse (1891): quoted by Hann.

Hann, R. G. (1902): *J. Obstet. Gynaec.*, **2**, 290.

Hirschberg (1910): *Z. Geburtsh. Gynäk.*, **67**, 526.

Hofstätter, R. (1922): *Med. Klin.*, **18**, 556.

Kennedy, W. J. (1882): *Edinb. med. J.*, **27**, 1085.

Levasseur (1873): quoted by Hann.

Mayer (1908): *Monatsschr. Gynäk.*, **184**, 4.

Pearson, quoted by Hann.

Priou (1865): quoted by Hann.

Underhill (1879): quoted by Hann.

The Aetiology of Congenital Torticollis and Certain Associated Deformities, with a Suggestion for Prophylaxis

BY

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No really satisfactory theory of the aetiology of congenital torticollis has hitherto been forthcoming. The main theories have been as follows:

(*a*) That the condition is due to some central neural defect Osler, 1912). No such defects, however, have ever been demonstrated in support of this theory.

(*b*) That the condition is an hereditary deformity (Krogius, 1924). This is no longer accepted.

(*c*) That the condition is due to intra-uterine infection (Kader, 1896). Proved cases of intrauterine infection are not accompanied by congenital torticollis. Histological studies do not support an infective theory.

(*d*) That there is prolonged obstruction to the venous return from the sterno-mastoid and neighbouring muscles during parturition. This results in venous infarction and the formation of the "sternomastoid tumour" (Middleton, 1930). The important work of Middleton and Brooke has received general acceptance, but the exact cause of the venous obstruction needs further elucidation. A "sternomastoid tumour" is not seen in all cases of congenital torticollis.

(*e*) This theory of venous infarction superseded an older view that the condition was due to arterial occlusion and ischaemia during delivery (Nové-Josserand and Viannay, 1906).

(*f*) That a uterine malposition is the real cause of congenital torticollis. This theory has had recent support from Chandler and Altenberg (1944), but without any explanation of what the malposition might be.

It is thus left to the obstetricians to confirm or refute this latter theory, and if confirmed to indicate what steps might be taken to prevent the occurrence of congenital torticollis.

With this end in view the antenatal and postnatal conditions of a number of babies born at Mercara Civil Hospital and elsewhere were correlated and viewed in the light of the literature on the subject.

In 53 cases, in all of which the head had been deeply fixed in the brim of the pelvis between 2 and 4 weeks before delivery, the ear which had been posterior showed slight deformity when compared with the anterior ear. Thus, in 28 cases where the back had been toward the right, the right ear was found to be affected. In 25 cases where the back had been towards the left, the left ear was affected. There were also 24 cases seen during the same period where the head had been deeply engaged for a period of 2 to 4 weeks, yet no difference between the 2 ears could be seen.

Thus there was a definite relation between these changes in the ear, when present, and the intra-uterine position of the foetus.

The deformities consisted of:

(*a*) Thinness and flabbiness of the auricle due to poorly developed cartilage, 43 cases.

(*b*) Flattening of the ear, especially of the helix, 53 cases.

(*c*) The softened helix had turned downwards as if by its own weight in 6 cases.

(*d*) The ear was either flatter against the head when compared with its fellow, or else protruded more. The latter was seen in 15 cases and seemed more prone to occur where the cartilage was especially thin. The former was seen in 48 cases. The protrusion or flattening of the ear was best seen when viewed from the back.

In addition 18 of these babies showed noticeable flattening of the supra-orbital ridge and adjacent part of the forehead on the side opposite to the deformed ear. This flattening of the supra-orbital ridge was best seen when viewed vertically from above.

Since in all these cases the head had been engaged in the pelvis some weeks before delivery it is necessary to consider the exact relationship of the foetal head to the pelvis when deeply engaged. Zweifel's frozen section (1893) of a woman who died at term showed quite clearly that the posterior ear was in relation to the promontory of the sacrum. Thus it seems clear that the minor alterations in the shape of the posterior ear seen in the cases described above were due to continuous pressure on the posterior ear by the promontory of the sacrum.

If one imagines the foetus in Zweifel's section to have engaged rather more deeply, the anterior supra-orbital ridge and adjacent forehead would have been in contact with the antero-lateral wall of the pelvis. This would no doubt explain the flattening of the forehead on the side opposite the affected ear in 18 cases.

It might be argued that such trifling differences between the 2 sides of a baby's face are of no consequence and that a large number of people have slight irregularities in their facial appearance. With this one would agree, except that these trifling changes are often associated with more severe deformities and point the way to an understanding of the aetiology and possible prevention of these.

The following 2 cases demonstrate the close relationship between the frequently occurring slight deformities of the ear on the one hand and the less common but more serious congenital torticollis on the other. If one accepts the view explained above that the pressure of the promontory of the sacrum frequently causes minor ear deformities, then it must also be accepted that if the head is still more deeply engaged there will be changes not only in the auricle but also in the adjacent area of the neck, that is, in the region of the sternomastoid muscle.

A primiparous European, aged 22, had a normal pregnancy and confinement. It was noticed that the head became unusually deeply engaged in the pelvis 4 weeks before delivery. The occiput, which was to the right, could not be felt and the sinciput could only just be felt, in spite of the fact that the patient was a thin woman who relaxed well. Labour, when it occurred, was easy and rapid. The child, a female, was not thought to have any gross abnormality, though a specially detailed examination was not made.

The mother, who was an intelligent woman, noticed soon after birth that the child's right ear was not as well formed as the left. It had a flattened appearance, was thin and flabby and protruded from the side of the head. She also noticed that the child seemed uncomfortable when lying on the left. When the child was a month old the mother realized that this was due to the fact that the child's head "was bent towards the right", which seemed to make it uncomfortable when lying on the left. Medical aid was then sought.

On examination the right side of the neck was seen to be more wrinkled than the left. The sternomastoid muscle was contracted and stood out prominently when put on the stretch. There was no "sternomastoid tumour". The head could be forced to the left only with difficulty.

The appearance of the ear was as described above. Its cartilage was markedly thinner than that of the other ear. The right cheek was flattened. The left side of the forehead and the left supra-orbital ridge were also definitely flattened.

The condition of the neck responded to conservative treatment of forcing the head over to the left twice a day. A cloth skull cap with ear pieces was worn at night to keep the protruding ear in position.

The asymmetry of the child's face could still be seen when it was 8 years old.

Two years later the mother gave birth to a male child. On this occasion the head again entered the pelvis some 8 weeks before the expected date of delivery, in the right occipito-anterior position. An accidental type of antepartum haemorrhage occurred however, and a child weighing 4½ pounds was born 4 weeks before the expected date of delivery. On careful examination of the baby's head and face, very slight inequalities between the 2 sides, similar to those seen in his sister could be made out. The sternomastoid muscles were normal. By the time the child was a few months old no trace of the facial asymmetry remained.

It is tempting to think that this baby, too, might have suffered from congenital torticollis but for the premature delivery.

A similar, though less striking case, was that of a Mohammedan woman who, 3 weeks after the birth of her first child, a male, brought it to hospital to have its septic umbilicus dressed. She had been delivered at home by a female doctor who, on questioning later, stated that the head had been unusually deeply engaged in the pelvic inlet some weeks before labour, and that the foetus had been in the left occipito-anterior position.

While the umbilicus was being dressed it was noticed, for the first time, that there was a mild degree of left-sided torticollis. The left side of the neck was more wrinkled than the right and the left sternomastoid stood out prominently when the head was straightened, which could be done only with difficulty, causing obvious pain. On further examination the left ear was found to be thinner and flatter than its fellow. The left maxilla and right supra-orbital region were flatter than on the opposite side.

With appropriate treatment the torticollis disappeared but after 6 months the facial and auricular inequalities were still recognizable.

One case of congenital torticollis was encountered which showed that on occasion the ear changes may be very severe.

A Hindu male, aged 26, applied for work at the hospital. It was seen that he was suffering from a moderate degree of right-sided torticollis, and severe deformity of the right side of his face and ear. He stated that he had been born with these deformities. He was the eldest child. None of his brothers or sisters had any abnormal appearance.

On examination the right sternomastoid was fibrosed and contracted. It stood out prominently when put on the stretch. The upper 1½ inches was much indurated. His face showed the usual stigmata associated with congenital torticollis, being comparatively undeveloped on the affected side. The distance between the outer angle of his right eye and the right angle of his mouth was only 2 inches whereas a similar measurement on the left side was 2¾ inches. The chin pointed to the sound side slightly. The mastoid process and maxillary process were both flattened on the affected side. There was, however, no difference between the 2 sides of his forehead.

The most striking feature of the case was the right auricle, which was represented by only a small fleshy lobule half-an-inch in length. There was no external meatus but on X-ray examination the bony meatus was seen to be present. A loudly ticking watch could be heard half an inch from the affected ear. Pressure over the bony meatus caused sharp pain.

It is interesting to note that though descriptions of congenital torticollis give adequate attention to the flattening of the face and forehead no mention seems to have been made of auricular deformities, although in the photographs accompanying such descriptions inequalities in the ears can sometimes be seen (Rose and Carless, 1927).

Out of Chandler and Altenberg's 101 cases of congenital torticollis, 3 had Erb's paralysis. Middleton likewise found congenital torticollis to be a not infrequent

accompaniment of this condition. These authors attribute the paralysis to traumatic delivery. Although trauma may be the cause in some cases it is far more likely that the same factors which caused the torticollis caused the Erb's paralysis too, that is, that the pressure of the sacral promontory catching the neck a little lower, was sufficiently prolonged to cause permanent damage to the upper trunk of the brachial plexus. Chandler and Altenberg had one case with a congenital short arm associated with congenital torticollis. Here the pressure must have been sufficient to interfere with the nutrition of the whole limb-bud, leaving it permanently shorter.

Discussion.

On the basis of the above considerations one can state fairly confidently that congenital torticollis, as well as certain associated conditions, is due to the continuous pressure on the parts when the head engages in the pelvis unusually early and deeply.

The "sternomastoid tumour" which sometimes develops 10 to 14 days after birth in association with congenital torticollis, is undoubtedly a secondary phenomenon and not the primary lesion as was once thought. Chandler and Altenberg consider it to be a fibroma forming in a muscle, previously damaged by intrauterine malposition, being traumatized during delivery.

Congenital torticollis is never bilateral. It occurs on the right side in 56.4 per cent of cases according to Eddy (1932) or 55.4 per cent according to Chandler. Since the back is usually on the left this right-sided preponderance requires some explanation. Presumably the well-known tendency for the occiput to be directed somewhat posteriorly when it is to the right, makes the sternomastoid muscle more likely to come directly in contact with the sacral promontory.

The head normally becomes fixed some weeks before term in a primipara. Thus a higher proportion of cases of torticollis amongst first babies is to be expected. Middleton found 43 of his 64 cases amongst first babies.

At first sight the comparatively large proportion of children with congenital torticollis who have been born by breech presentation might appear to be inconsistent with the views expressed above. How could such cases have been caused by pressure of the sacral promontory on the child's neck? Chandler and Altenberg, who found 30 cases of breech presentation amongst their 101 cases of congenital torticollis, suggest that intrauterine torticollis prevents engagement of the foetal head. It is well known that the foetus changes its position frequently, and having once developed torticollis in the manner described above, should the head then disengage, the torticollis might well militate against re-engagement of the head, thus favouring the assumption of the breech position.

The possibility of preventing congenital torticollis and associated conditions.

Where the head is found unusually deeply engaged in the pelvis during the 36th week or earlier and remains in this position, it might well be that induction of labour some weeks early might prove beneficial. Further work will be required before any definite indications for induction of labour for this condition could be given.

In any case after delivery in such circumstances a careful inspection of the baby is necessary to exclude torticollis, Erb's paralysis, etc. Congenital torticollis is easily missed during the first months of life,

while the earlier treatment is commenced the better.

Conclusion.

The close relationship between certain congenital abnormalities of the ear, congenital torticollis and some cases of Erb's paralysis is demonstrated.

From a study of a series of patients and the literature on the subject it is concluded that these conditions are due to the foetal head and neck entering the pelvis earlier and more deeply than usual before labour, where, having lost the protective cushion of the amniotic fluid, the parts are subjected to continuous pressure chiefly by the promontory of the sacrum.

Prophylaxis by induction of premature labour is a possibility.

In all cases where the foetal head has been unusually early and deeply engaged, the baby's head and neck should be very carefully inspected at birth to make sure that mild cases of torticollis or Erb's paralysis are detected.

References.

Chandler, F. A., and Altenberg, A. (1944): *J. Amer. med. Ass.*, **125**, 476.

Eddy, H. C. (1932): *Amer. J. Surg.*, **17**, 100.

Kader, B. (1896): *Beitr. klin. Chir.*, **17**, 207.

Krogius, A. (1924): *Acta. chir. scand.*, **56**, 497. (Quoted by Chandler and Altenberg).

Middleton, D. S. (1930): *Brit. J. Surg.*, **18**, 188.

Nové-Josserand, G., and Viannay, C. (1906): *Rev. Orthopéd.*, **7**, 397.

Osler, W. (1912): *Principles and Practice of Medicine*. London, p. 1052.

Rose, W., and Carless, A. (1927): *Textbook of Surgery*. London, p. 471.

Zweifel, P. (1893): *Die Symphyseotomie*. Leipzig. Reproduced in Stander (1941). *Williams' Obstetrics*. New York.

The Treatment of Intractable Cases of Essential Pruritus Vulvae

BY

ADALBERT HORN, M.D.

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THE problem of the pathogenesis and therapy of pruritus vulvae cannot be regarded as yet solved. This fact explains the innumerable methods of therapy. In most cases pruritus vulvae does not imply a serious disease. Its severe forms, however, cause great suffering to the victims to such an extent that their social intercourse and especially their rest is disturbed.

The essential symptom is an itching and burning feeling in the vulva and its vicinity, and in many cases in the region of the anus as well, and may be intermittent or continuous.

According to the classification generally used in the literature there are 2 separate forms of the disease: (1) the symptomatic (exogenous) pruritus which appears as an accompanying symptom of other diseases; (2) the essential (primary) form which represents a true disease entity.

The pathogenic factors and therapy of symptomatic pruritus vulvae are generally known. The problem is presented by the essential (primary, endogenous) form as there are cases of this disease which do not respond to any local or general treatment whatever. These cases are a real "crux medicorum" causing great suffering to the patients and presenting a big problem for the medical attendant.

In a number of cases the pathogenic factor cannot be identified even by the most thorough investigation, and difficulties are increased by the fact that a combination of factors is present in some cases. In these only symptomatic treatment can be applied and if this is protracted a vicious circle is created, itching followed by scratching and energetic scratching increases itching.

The method described below would appear to be original as there is no data in accessible literature as to its previous use. It has some resemblance to Ball's procedure (1905) which, in cases of pruritus ani, makes semicircular incisions on both sides of the anus and undermines the edges of the wounds. Caroll W. Allen (1920) makes radial incisions around the anus and puts iodoform gauze under the "skin-ribands," removing it after a week, thus preventing the skin from adhering to its base.

Before describing the procedure I want to emphasize that it is essential to exclude the existence of local pathogenic factors by the most thorough investigation before surgical intervention, and also to make the point that proper application of the procedure described below is restricted to cases of essential pruritus and is not advisable in cases of kraurosis vulvae.

The operation is performed as follows. After thorough identification of the itching area the whole diseased skin-surface is infiltrated subcutaneously with 0.5 per cent novocaine-adrenalin solution. Thereafter a number of 2 cm. long transverse incisions are made. It is advisable to make the incisions in a certain succession. The

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

A.H.

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procedure described below shows the method used in cases in which pruritus affects the mons veneris, the vulva and the anal region as well.

Through the incisions, by means of scissors with thin, slightly bent blades, frequent cuts are made subcutaneously in order to separate the skin from the underlying tissue which is within reach. The first incision is made 2 cm. above the tip of the coccyx (Fig. 1). From this incision the skin of the posterior perineum can be separated up to the mucous membrane of the rectum. An incision is made medial to the ischial tuberosity on each side (Fig. 2). From these incisions the upper part of the anal region, the perineum and the lower parts of the labia majora and minora can be reached. Incisions are made on each side of the labia majora (Fig. 3). From here the rest of the labia majora and minora and the region of the clitoris are accessible. The mons can be reached by long-handled scissors from these incisions. If need be an incision may be made above the clitoris in order to separate the skin of the mons and around the clitoris. The number of incisions depends on the extent of the itching area.

After finishing separation of the skin each incision is immediately sutured (Fig. 4). The subcutaneously injected novocaine-adrenalin solution temporarily prevents bleeding; minor or major subcutaneous haemorrhages, however, cannot be avoided as a consequence of the operation. Serious haemorrhages, however, have not been experienced. These subcutaneous haemorrhages actually increase the effect of the operation by separating the skin from its base during the time of absorption. Great importance is attached to postoperative treatment of the separated skin. The greatest need is to keep the skin dry by frequent sprinkling with neutral powder. No bandage is applied. Owing to abolition of scratching the excoriations heal in a very short time. On the first days after the operation a slightly painful and burning feeling usually develops and for that administration of an anodyne is necessary.

The first operation was performed in August 1945, and since then 8 patients have been operated on in this way: in 7 cases as separate operations and in 1 case (kraurosis vulvae) as a supplementary operation to vulvectomy. In this case itching extended around the anus and after vulvectomy the skin of the anal region was, therefore, also separated from its base.

Prior to the above operation these cases were treated unsuccessfully by numerous methods. Two years was the shortest time during which the patients suffered from pruritus vulvae. In one case the pruritus was treated for 20 years without improvement. After operation the pruritus promptly ceased and the patient has not complained since.

All the patients have been similarly treated and the complaints were of the same nature, thus it is sufficient to give the record of only one case. She was the first to be operated on by this method.

Case Record.

Mrs. T. M., aged 51; Menarche 16. Since then menstruation every 21st day, lasting for 4 to 5 days. No cramp, last period in 1939. She had had 1 normal delivery and 2 spontaneous abortions.

Two years ago pruritus began on the vulva. Since then constant itching, increased chiefly at night. Prior to admission she was given folliculin (70 mg.) and received X-ray irradiation. No improvement was obtained. She was suffering from intolerable nervousness.

Condition on admission. Emaciated patient; no palpable abnormality in the abdomen. Urine normal. Red-blood cells, 4,300,000. White-blood cells, 7,000. Sedimentation of red-blood cells, 16 mm. in 1 hour. Dellamartina-Mester reaction showed no deficiency of vitamins. Gynaecological examination showed no abnormalities except

excoriations on the vulva. Owing to the bad nervous state of the patient and the failure of the previous treatment, the operation was performed. After operation itching ceased immediately, and on the 5th day with well-healed wounds the patient was discharged and had no complaint whatsoever. Fortnightly and subsequent monthly control examinations were made, and after 17 months the patient was still free of symptoms.

All of the cases operated on in this way healed promptly and it can be stated that the cure may be regarded as permanent—the first operation having been performed 20 months ago.

Conclusions.

The surgical intervention described above copes with the task of curing cases of essential (primary) pruritus vulvae which do not respond to the usual treatment. The procedure has the advantage of being a minor intervention unaccompanied by risk, the curative effect is instantaneous, and entails only 5 to 8 days in hospital. In conformity with the extent of the itching parts the separation of the skin may be extended within wide limits.

It is realized that the small number of cases is not sufficient to allow final conclusion as to the value of the procedure. However, the good results obtained recommend its further application.

References.

Allen, C. W. (1920): *Med. surg. J. New Orleans*, 73, 127.

Ball, C. (1905): *Brit. med. J.*, 1, 113.

Dicephalic Monster

BY

STANLEY NOWELL, M.B., F.F.R.

AND

R. OWEN-JONES, M.B., F.R.C.S.

Wrexham.

THE present case is being reported as the abnormality was clearly defined by X-rays beforehand, and the delivery was by a pre-selected Caesarean section.

The case was referred to one of us (S.N.) for radiological examination to confirm the presence or absence of twin pregnancy.

On examining the films 2 foetal heads were seen lying close in the fundus (Plate I), one being anterior to the other in the lateral view. Two vertebral columns were visible, but these were noticed to be lying close together and parallel, diverging somewhat in the cervical region. The appearance raised the possibility that there was a fused foetus present and not twins. An oblique view of the lower abdomen confirmed this conclusively (Plate II). A single foetal pelvis was clearly seen, with 2 vertebral columns ending in 2 sacra, lying between a right and left ilium. It was also apparent that there were only 2 foetal legs and 2 developed foetal arms present. The upper interskeletal ribs between the 2 vertebral columns were fused together.

On the evidence, a report was given to the practitioner in charge of the case that there was a partially-fused foetus present, thoracopagic in type. In view of these findings the second of the writers (R.O.J.) was called in for consultation.

The patient was examined at the 36th week of pregnancy. She was a primipara of 34. Both she and her husband were "disconcertingly normal" (Malpas, 1937). The patient's grandfather was one of twins, this being the only point of interest in the family history. She had had no illness in the early weeks and indeed remained perfectly healthy throughout the pregnancy. The uterus corresponded in size with a single pregnancy at date, but the fundus was markedly widened. Hydramnios, pressure oedema or any toxic signs were absent.

The two heads in the fundus were proximate but could be fairly easily separated about 3 inches. It is interesting to note, in view of the subsequent findings, that a different foetal heart rate of 6 per minute taken simultaneously by 2 observers was noted (apparently from 2 foetal hearts). The pelvis was adequate on clinical examination.

A Caesarean section was performed at the 37th week. The aftercoming heads were easily delivered separately through an average lower segment incision (Plate III). Both inspired immediately on delivery of the heads, with strong pulsation of the single cord of normal length, centrally inserted in a normal placenta. It was impossible to observe whether the second head inspired *in utero* on delivery of the first. For the first few minutes the inspirations were simultaneous but then became less synchronous. As one inspired, the other immediately followed suit. The outer common carotids in both beat strongly and

synchronously. On separation of the heads the inner carotid pulsations were difficult to observe and palpate. The faces were identical, both blinked normally and separately. The right head was facetted in the temporal area by the left one which was slightly larger in all diameters. The fontanelles and sutures were normal for the stage of maturity. The heads shared the body evenly on the wide shoulders. Posteriorly, at the acromial level, there was a fixed protrusion bearing a marked resemblance to the hump of a well-known humorous literary character (Plate IV). The monster passed some urine through a normal penis. Nothing abnormal was noted in the rather massive arms and smallish legs. It survived about 20 minutes and apparently died physiologically altogether.

Its birth weight was $7\frac{1}{4}$ pounds. The combined bi-parietal diameter was 19 cm., and the bisacromial 17 cm.

After delivery, further radiological examinations were made of the foetus. This confirmed the skeletal appearances demonstrated on the films taken before delivery.

The upper 7 ribs, between the 2 vertebral columns, were seen to bow upwards and were fused together in the midline, with a rudimentary scapula at the extreme upper end.

To study, grossly, the vascular system, Diodine solution was injected into the right foetal common iliac artery (Plate V). At first 6 ml. were injected. This ran up this vessel into a vessel running alongside the right vertebral column. This latter vessel joined on to the lower part of the left-sided aorta at L.4 level.

There was only 1 heart lying in the thorax almost centrally between the 2 foetuses. From this the aortic arch rose into the left foetus and descended normally to the lumbar region. From the arch arose an innominate and left common carotid artery. At the lower end of the left aorta a left common iliac artery was seen. The right aorta arose from the left one at L.4 level and ran up alongside the right vertebral column, presumably supplying the right head and neck.

After 20 ml. had been injected a single superior and inferior vena cava were seen.

To study the gastro-intestinal system a catheter was passed down each oesophagus and thin barium was injected down each catheter (Plate VI).

The right oesophagus appeared to end blindly at D.2 level, the catheter doubling back at this level and no barium passing lower down. The left-sided oesophagus passed into a normal-looking stomach situated normally in the left side of the abdomen. Some of the barium passed into the upper small intestine, which was lying on the right side of the two foetuses. Presumably, therefore, there was a common gastro-intestinal system below the diaphragm for the two foetuses.

Since 1900, 47 cases of dicephalic monsters have been reported. So far as can be traced 2 of these were radiologically diagnosed antenatally (Hunter, 1941; Brailsford, 1942). In the second of these an almost identical foetus but with 2 central rudimentary arms is illustrated. It is not stated whether this fusion was discovered antenatally but presumably it was, since Brailsford (1944; 1942) draws attention to the great importance to the obstetrician of recognizing such a fusion before birth. He also draws attention to the antenatal signs suggesting fusion, e.g. heads bearing similar relation to the trunks, spines parallel to each other and abnormal interskeletal ribs. Such signs are clearly seen in the present case. One only of these cases (Brailsford, 1944) was delivered by Caesarean section, having been clinically diagnosed as probable twins, the indication for the abdominal method of delivery being an antepartum haemorrhage at the 36th

PLATE I.
Postero-anterior View.

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PLATE II.
Tilted View to Show Foetal Pelvis.

N. & O.-J.

PLATE III.
Anterior View.

N. & O.-J.

PLATE IV.
Posterior View.

N. & O.-J.

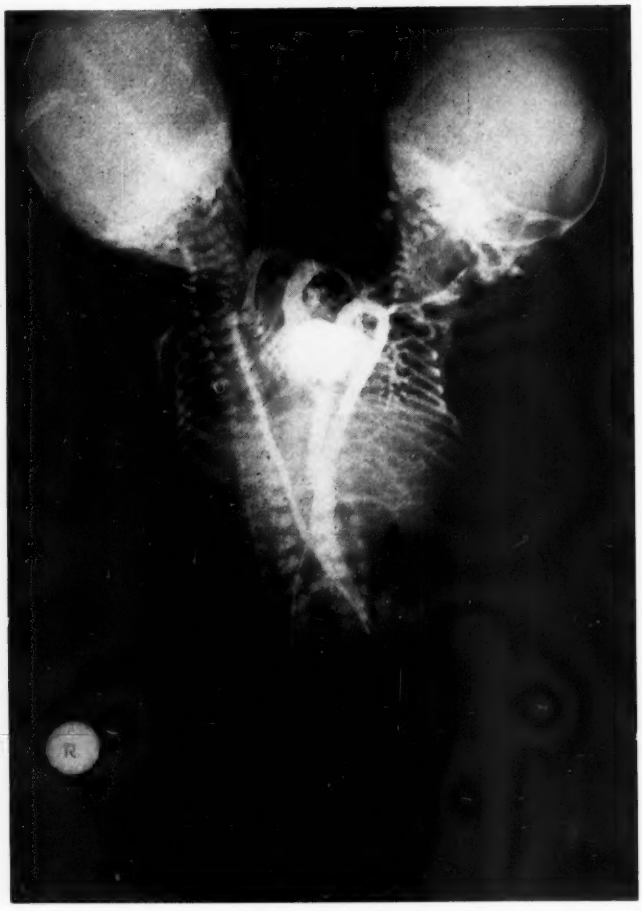

Plate V.

Arterial System after 20 ml. Diodine.

N. & O.-J.

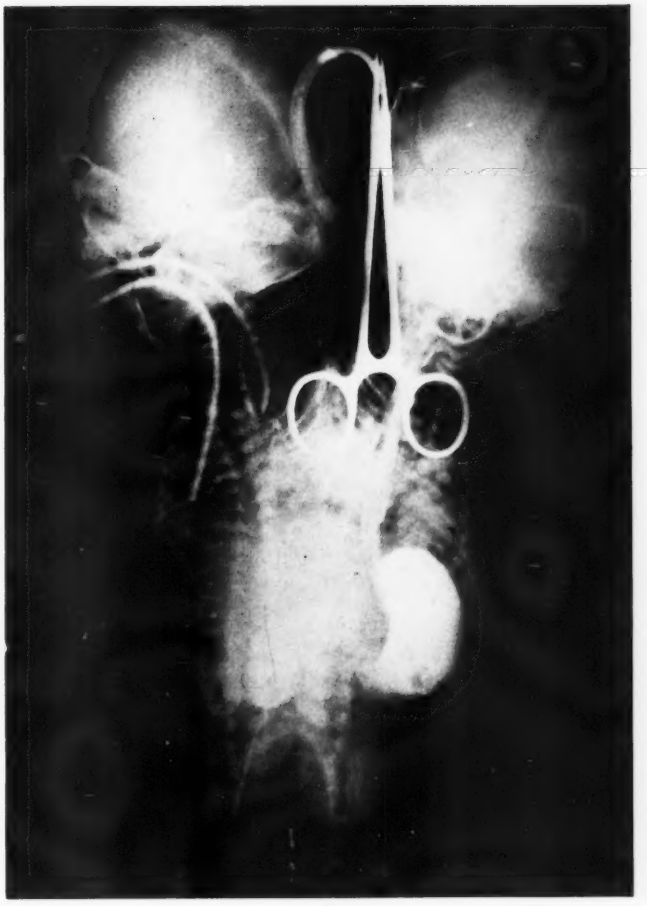

PLATE VI.

Barium in Oesophagus and Stomach.

N. & O.-J.

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week. In the present case it would have been possible to deliver vaginally in spite of the wide shoulders. Stander (1945) refers to the fact that the first head and then the second head can be extracted if a breech. The free lateral movement of the heads in this case might have allowed this if the 2 aftercoming heads did not try to engage together. The decision to deliver abdominally, however, has left us with a patient with an undamaged birth passage and she has been advised that, in view of the great rarity of the condition, there is no contra-indication to further pregnancy.

After the various postmortem investigations referred to were carried out, it was appropriately sent to the Bland Sutton museum at the Middlesex Hospital.

We are especially indebted to Dr. A. M. Thomas, who took the photographs, to the Librarian of the British Medical Association, and to the anaesthetist and residents at the Wrexham Hospitals.

REFERENCES.

Brailsford, J. R. (1942): *Brit. J. Radiol.*, August, p. 222.

Brailsford, J. R. (1944): *Radiology of bones and joints*, p. 6, fig. 4. London.

Hunter, (1941): *J. Obstet. Gynaec.*, **48**, 251.

Malpas, P. (1937): *J. Obstet. Gynaec.*, **44**, 438.

New York.

Stander, H. J. (1945): *Williams' Obstetrics*, p. 918.

Haemorrhagic Disease of the Unborn

BY

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Obstetrician, Hillingdon County Hospital, Middlesex.

HAEMORRHAGIC disease of the newborn is a well-known entity, characterized by bleeding, chiefly from the bowel, due to prothrombin deficiency at birth.

Bleeding is usually first noticed from the bowel, from the first to the fourth day of life, and is shown by the presence of bright blood or by a tarry stool containing altered blood. This first tarry stool is sometimes mistaken for ordinary meconium, as it occurs usually about the time when the character of the stool is changing from meconium to normal yellow.

Bleeding can occur from any of the mucus surfaces, or under the skin, and sometimes the onset is so severe that the infant dies before any treatment can be given.

The peculiar interest of the case described here is that the disease was discovered before birth.

The details are as follows:

A primigravida, aged 34, had been married for 10 years. She attended the antenatal clinic regularly, and to her delight was found to have a twin pregnancy.

At the 36th week she developed signs of toxaemia with a sudden rise of blood-pressure to 170/100 and with oedema of the legs. She was brought into hospital for rest and her blood-pressure dropped to 128/80.

X-rays showed the first twin to be presenting by the breech and the second by the vertex.

Labour commenced spontaneously at the 37th week at 10 a.m. on March 12th, 1947. Four hours later the patient was reported to be passing meconium in the vaginal discharges. On examination it was seen that this meconium was a typical tarry stool of haemorrhagic disease of the newborn, and that it also contained a little bright blood. A portion was sent to the laboratory for confirmation. At this stage the pains were strong, the os was only slightly dilated, and the breech was above the brim.

The mother was given omnopon, gr. 1/3; scopolamine gr. 1/150; and Prokayvit (vitamin K) 20 mg.

After 1½ hours, at 3.30 p.m., there was the passage of still more blood from the infant, and the foetal heart dropped to 80. There was no other cause found for foetal distress. About 120 ml. of the tarry material had been passed by this time.

It was considered that if labour were to continue normally the first child would die from haemorrhage before it could be delivered, but that immediate Caesarean section, followed by blood transfusion might save the infant.

The position was explained to the mother, who at once agreed to any measure that would give a chance of the child being saved.

At 4 p.m. a lower segment Caesarean section was performed under cyclopropane anaesthesia. The first twin was very limp at birth, and was given an immediate transfusion of 40 ml. blood with 10 mgm. of Synkayvit (vitamin K) into the cord. The second child was healthy. These were binovular twins, the first being female and

the second male, with birth-weights of 4 pounds 9 ounces and 5 pounds 5 ounces. Some tarry meconium was still present around the anus of the affected child at birth and rectal examination confirmed the presence of blood in the rectum.

The infant was given 10 mgm. of Synkayvit daily.

On the fourth day there was a second small tarry stool, but, after this, no further bleeding. The birth-weight was regained by the thirteenth day, and the mother and both infants were discharged on the twentieth day. The mother made an uninterrupted recovery.

The interesting features of this case are the occurrence of bleeding before birth, in one only of binovular twins, with recovery after delivery by Caesarean section followed by blood transfusion.

A similar case, with less fortunate ending, is also described below:

Mrs. D., aged 26, was a primigravida who was healthy and who had an uneventful pregnancy. She came into labour at term, and labour progressed normally. At full dilatation, after a first stage of 6 hours, the foetal heart was regular and clear. The membranes did not rupture but presented at the vulva and were ruptured artificially. Just before rupture, the foetal heart was 120, but 10 minutes afterwards the heart sounds disappeared completely. The infant was born by natural forces 10 minutes after the heart sounds ceased. There was a gush of bright red blood as the head was born. At birth the infant was apparently dead. It was absolutely white, and bright red blood was pouring from its mouth and nose. As the blood was cleared with a mucous catheter more blood appeared. It was unlikely to have been inhaled, because the infant had never breathed.

Lobeline and coramine were injected into the cord and respiration commenced after about 5 minutes. The heart was beating very faintly. The child was limp and toneless, and made no effort to move or cry. A little fresh bright blood still appeared through its nose, and it was agreed that it was suffering from haemorrhagic disease of the newborn—a massive haemorrhage having probably occurred just before birth, after which the foetal heart had ceased.

A blood transfusion was given about half-an-hour after birth. Group O Rhesus negative blood 5 ml. were given into the cord. No more blood would run into the cord, therefore a further 10 ml. were given into an arm vein and 10 ml. were also given intramuscularly into each buttock.

The child's condition improved considerably. A faint pink tinge of the skin appeared, the conjunctivae became deeper pink—having previously been colourless—and muscle tone improved sufficiently for the infant to resist the intramuscular injections. Breathing was still shallow, and the heart was feeble. The child was left in its cot to rest and recover, but during the night it had another small haemorrhage and died.

Postmortem examination showed considerable fresh bleeding in the duodenum and upper part of the jejunum. There was no evidence of ulceration.

Obituary

CHARLES PHILIP BRENTNALL

M.C., M.B., Ch.B., F.R.C.O.G.

C. P. BRENTNALL died in Manchester on June 26th, at the age of 56. Son of the Rev. Edward Brentnall, M.A., he received his early education at St. Paul's School, London, and the Manchester Grammar School and then, having gained the Dreschfeld Scholarship, proceeded to Manchester University to study Medicine. Whilst in his second year his father moved to a living in West Lancashire, so Brentnall transferred to Liverpool University. There he had an unusually brilliant career, gaining Distinction in the M.B. Examinations in Anatomy, Pharmacology and Pathology, and also winning the Gee Prize.

He qualified in 1915 and after holding the post of House Surgeon to the Liverpool Northern Hospital joined the Royal Army Medical Corps. He served in the field in Gallipoli, Palestine and France, rose to the rank of Major and was awarded the Military Cross. After the war he returned for a time to work in Liverpool and was then appointed resident to the Hospital which he served for the rest of his life, St. Mary's, Manchester. At St. Mary's he was successively House Surgeon, Resident Obstetric Officer, Resident Surgical Officer and Registrar, and was elected to the Honorary Staff in 1925.

Brentnall's work as a gynaecologist was typical of the man. His approach was gentle. In consequence his surgical results were outstandingly good and his technique served as a model for his juniors. As was to be expected, he built up a large consulting practice and his services were in demand over a wide area. His appointments outside Manchester included those of Honorary Obstetrician to the Stretford Memorial Hospital and Honorary Consulting Gynaecologist to the Warrington Infirmary.

A Foundation Member of the Royal College of Obstetricians and Gynaecologists, he served on the Council for 6 years, being raised to the Fellowship in 1938. He was also a member of the Gynaecological Club.

Brentnall's contributions to gynaecological literature were made largely in the form of communications to the North of England Obstetrical and Gynaecological Society of which he was a Fellow. A regular attender of meetings he could always be counted upon to add something of interest to a debate or to give a word of encouragement to a junior member. It was indeed tragic that shortly after his election as President he should have been stricken by the illness from which he eventually died. During recent years he has published 3 papers in the *Journal of Obstetrics and Gynaecology of the British Empire*: "Local anaesthesia in vaginal operations"; "Arrhenoblastoma of the ovary during pregnancy"; and "A note on Fothergill's Colporrhaphy."

In his private life Brentnall was singularly fortunate and he was never so happy as when in his own home he could enjoy the companionship of his family and friends. He leaves a widow, a daughter, and a son who is studying medicine.

CHARLES PHILIP BRENTNALL

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At the meeting of the Council held on May 31st with the President, Mr. W. Gilliatt, in the Chair, it was announced that Field Marshal the Rt. Hon. Jan Smuts, P.C., had accepted an invitation to become an Honorary Fellow.

To mark the grant of the Royal Charter of Incorporation by H.M. the King on March 21st the four surviving signatories to the Articles of Association, whereby the College was founded, were elected to the Honorary Fellowship:

Professor J. M. Munro Kerr.
Professor C. G. Lowry.
Sir Ewen Maclean.
Sir William Fletcher Shaw.

The following were elected to the Council to replace those retiring in statutory rotation:

As Representatives of the Fellows—

Dugald Baird, Aberdeen.
Alice Bloomfield, London.
Gilbert Innes Strachan, Cardiff.

As Representatives of the Members—

John A. Stallworthy, Oxford.
Arthur M. Sutherland, Glasgow.
Robert James Wotherspoon, Glasgow.

A Standing Committee of the Council to be known as the Australian Regional Council has been set up in Australia. Dr. F. A. Maguire, of Sydney, has been appointed Chairman. The Australian Regional Council will act as a representative Committee of the Council of the College in discussions and negotiations affecting the practice of obstetrics and gynaecology in Australia. Professor B. T. Mayes, of Sydney, will act as Honorary Secretary of the Australian Regional Council.

The following were admitted to the Fellowship of the College:

Malcolm Duncan Black.
James Stoddart Hevell.
Jerusha Jhirad.
Thomas Nicol MacGregor.
Robert Newton.
George Drury Shaw.
Gerald Spence Smyth.
Harry Silvester Waters.
Bryan Williams.

The following were admitted to the Membership of the College:

Duncan Ballantine.
Margaret Rosalin Biggs.
William Stewart Campbell.
John Barr Cochrane.
Sydney Joel Cohen.
Henry Vincent Corbett.
Albert Davis.
John Roscoe Dickinson.
Bessie Dodd.
Morag Dods.
Robert Chalmers Gill.
Jean Lilian Hallum.
Ronald Fox Lawrence.
Thomas Henry Lawton.
John Malcolm McBride.
Reginald Arthur Edward Magee.
Michael Kieran O'Driscoll.
Stewart Sandeman Favell Pooley.
Louis James Quinn.
Robert Burnett Salter.
Philip Cedric Thomas.
Kathleen Mary FitzGerald Worrall.
James Lawrence Wright.

A Meeting of the Council was held in the College House on Saturday, 26th July, 1947, with the President, Mr. W. Gilliatt, in the Chair.

Mr. W. Gilliatt, C.V.O., M.D., M.S., F.R.C.P., F.R.C.S., P.R.C.O.G.; was re-elected President.

The following officers were also re-elected:

Vice-Presidents.

Sir William Fletcher Shaw, M.D., M.M.S.A. (Hon.), F.R.C.O.G.,
James M. Wyatt, F.R.C.S., F.R.C.O.G.

Honorary Treasurer.

Arthur A. Gemmell, M.A., M.D., F.R.C.S.E., F.R.C.O.G.

Honorary Librarian.

F. W. Roques, M.A., M.D., M.Ch, F.R.C.S., F.R.C.O.G.

Honorary Curator to the Museum.

Aleck W. Bourne, M.B., B.Ch., F.R.C.O.G.

H. G. E. Arthure, M.D., F.R.C.S., M.R.C.O.G., was elected Honorary Secretary.

The following Candidates were elected to the Membership of the College:

Segulla Jacob Aptekar.
Henry Bernard Bagshaw.
George Henry Bancroft-Livingston.
Solomon Bender.
Isabella Russell Bishop.
James Tweedie Swan Brown.
Gwendoline Eardley Cockren.
James McDiarmid Corston.
George Archibald Craig.
Kenneth Joseph Robson Cuthbert.
Rudolph Walter Danziger.
Burjor Cavas Dastur.
Josephine Alice Davidson.
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Eric Eli Rawlings.
Elisabeth Margaret Rose.
Dorothy May Satur.
David Arnold Fletcher Shaw.
Denys John Neal Smith.
James Walker.
Ada Sau Wong.

BOOK REVIEWS

"Antenatal and Postnatal Care." By FRANCIS J. BROWNE. Sixth edition, 1946. Churchill. 644 pages; 90 illustrations. 24*s*.

To the reviewer's mind this is the most valuable book of its kind in any language. Its information is both comprehensive and considered; it is a "safe" book from the points of view both of candidates for higher obstetric degrees and for the general practitioner who must meet the obstetric emergency from time to time. Both the ideal and the practicable are preached; in these days Browne shows that the two can usually be identified. The ground surveyed is immense; there is very little of importance in the whole field of obstetrics that is not admirably discussed. Special praise must be given to the section on general diseases of the pregnant woman, and particularly to the management of cases of diabetes, thyrotoxicosis and heart disease.

The treatment of abortion is particularly well considered. Despite recent pronouncements in the medical press, the reviewer's own extensive experience of septic abortion suggests that Browne's advocacy of conservative treatment is still the best even in this era of the sulphonamides and penicillin. Professor Browne is a world-acknowledged expert on the toxaemias of pregnancy—the chapters dealing with the subject are the latest word and written with unusual grace and lucidity.

Trial of Labour is very well discussed and this knotty subject very fairly considered from every angle and opinion. If detraction be permissible, the reviewer would like to advise that the italicised "definition" of Trial Labour on page 296 should be removed. Given such prominence it is bound to be remembered as authoritative although the rest of the section shows how rarely this definition obtains and how fraught with disaster is its rigid adoption. The reviewer rejoices that Professor Browne himself considers premature rupture of the membranes virtually to cancel the trial.

The chapters on pyelitis are among the best in the book. The aetiology, diagnosis and course of the disease are authoritatively discussed; the reviewer must, however, deplore the recommendation in this widely read and respected publication of quite unnecessarily large doses of sulphonamides for the treatment of the infection. From trial in the laboratory and in clinical practice both here and in America it has been shown again and again that a maximum of 1.5 to 2 g. of the chosen sulphonamide in 24 hours is all that is necessary. The kidneys in pregnancy are not in such a state as to be called upon to excrete massive doses of a drug which is peculiarly prone to cause renal damage. We hope to see this considered in future editions. If these small doses (1 tablet of 0.5 g. three times a day) fail, either the patient has vomited the drug, which should then be given hypodermically, or renal anatomy or pathology of an obstructive nature exists and should be remedied.

Sulphathiazole, which Professor Browne recommends as a more strongly bacteriostatic agent in serious cases should *never* be used in renal infections as, with sulphapyridine, it has the worst reputation for the production of crystalluria.

Antenatal and Postnatal Care is written throughout in a most attractive style which must account, apart from the great value of the matter, for the extraordinary affection in which the book and its author are held throughout the English-speaking world. Apart from the pleasure the manner of the book gives to those whose mother tongue is English, the reviewer has been told again and again of the ease with which the author's sense can be grasped by the foreign, and especially the oriental, student, who usually appreciates the merely didactic.

"The Rhesus Factor." By G. FULTON ROBERTS, M.A., M.B. W. Heinemann, Medical Books, Ltd., London. 3*s*. 6*d*.

THERE is without doubt a great demand for a lucid summary of knowledge about the Rh Factor. Unfortunately there are few people who are in a position to write a comprehensive and authoritative account, for it should include sections on the

theory and genetics of the factor, on its clinical significance, and on the serological tests for its various antigens and antibodies. Developments have been so rapid that only a person actively engaged in research in all these fields is likely to be able to assess correctly the value of each different new contribution and to form from the mass of data a clear and true picture of the whole.

The present book, which is very short, gives a good elementary account of the theory of the subject and of its clinical importance.

One is very pleased to find an exposition of Fisher's CDE nomenclature, but sorry to see it relegated to a subordinate position. Most teachers, both in this country and, apparently, in the United States and elsewhere, are finding that Fisher's scheme is the only one which can be easily expounded. The original symbols introduced by Wiener are very convenient for use in speech but, since they only allot a single sign for a complex of antigens, their relationship to one another is very difficult to explain and harder still to commit to memory. Fisher's scheme, with its use of single letters for single antigens and thus of combinations of letters to describe genes, is cumbersome but far more easily understood.

With regard to the clinical side of the book, the main facts are clearly set out and illustrated by useful case-histories, and the treatment of the infant affected with haemolytic disease is described. With regard to the latter, one feels that the author has perhaps not quite a large enough personal experience to be able to write a really satisfactory account.

One may summarize the book by saying that it is a useful introduction to the subject; but it must be added that a person who has mastered the elements and wishes to obtain authoritative, up-to-date information on any of its manifold aspects must still be given a list of references to recent medical journals.

P. L. MOLLISON

"Textbook of Obstetrics." By GILBERT I. STRACHAN, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G., with 3 colour plates and 323 illustrations in the text. London: H. K. Lewis & Co., Ltd. 1947. Price 45*s*.

THE publication of this new textbook of obstetrics from the Welsh National School of Medicine and dedicated by the author to his friend and colleague Sir Ewen Maclean may well be regarded as an event in British obstetrics. It is not, as so many textbooks are, written by one at the outset of his professional career but by an obstetrician and teacher of ripe experience who has served a long apprenticeship to his specialty, who is rightly regarded by his colleagues as a leader in his profession and who has himself contributed largely to knowledge of its theory and practice. In the words of his preface the book embodies "the experience of many years of teaching and practice in this specialty . . . while the opinions of others have been freely referred to, the personal aspect of the matter has been stressed . . . one thing has been emphasized throughout the book, namely, the importance of conservatism, and the avoidance of unnecessary interference, the policy of hands off." The book, considering the stringency of the times, has been remarkably well turned out by the publishers, the illustrations are numerous, and mostly original, and we have been unable, in spite of careful perusal, to discover more than one or two misprints. To get this less pleasant part of the business over and done with we would point out that the genitive "pubis" is used more than once instead of the nominative "pubes", that "ventri suspension" should be "ventro suspension" and that, especially in these days of paper shortage, we do not like the expression "full term."

It is a pity that where so many references to literature are given there is no bibliography. Might we suggest that this want should be supplied, preferably at the end of each chapter in the next edition? This is because in our opinion the book will appeal not only to harassed students preparing for final examinations but to a far wider circle of readers including many preparing for higher examinations, and who may therefore wish to consult original papers.

In a book so generally excellent there are few subjects for criticism. It is noteworthy, however, that Professor Strachan still thinks that the normal true conjugate of the pelvic inlet measures 4 inches (10 cm.). This is all the more strange as it is evident from the text that he is well acquainted with the work of Hastings Ince and Matthew Young. These workers made a radiological survey of the pelves of 500 consecutive women in the antenatal clinic at a London hospital. One of their

most important findings was that the mean length of the true conjugate was 4½ inches. In diagnosis of contracted pelvis no mention is made of the importance of measuring the patient's stature, a very simple procedure that takes little time and yet gives useful information. If it is under 5 feet contracted pelvis is often though of course not invariably present. In the description of the measurement of the diagonal conjugate it is advised that the patient should be on her back. If she is on her left side with her knees well drawn up it is possible to press the perineum much farther back and even in a normal pelvis to reach the sacral promontory with the examining finger. The section on placentation is excellent and well illustrated, as would be expected from one who has himself published two standard monographs on the physiology and pathology of the placenta.

The chapter on placenta praevia contains sound teaching. It is good to note that the use of the terms first, second and third degrees of placenta praevia is advised rather than the confusing terms lateral, marginal, etc. The value of expectant treatment is emphasized but no mention is made of the advisability of passing a speculum as soon as possible after admission in order to inspect the cervix and exclude certain extraplacentral causes of bleeding, especially cancer of the cervix. The procedure is simple and does not entail any risk of introducing sepsis or causing further haemorrhage. In the treatment of contracted pelvis Professor Strachan advocates trial labour in contradistinction to inducing premature labour. The reasons he gives for this are that, first, unnecessary inductions are often done, and, secondly, that the neonatal death-rate amongst the premature infants obtained by induction is high. One wishes that the foetal and neonatal mortality from trial of labour in Cardiff had been given. We have the impression that in general it is lamentably high and in one large series quoted in the American literature it is 20 per cent in cases where the labour had lasted 30 hours or more. It is doubtful if this can be much reduced except by doing more Caesarean sections either with or without a preliminary test of labour. If induction of premature labour were, like test of labour, only carried out in the best surroundings by those with special experience in the diagnosis and management of contracted pelvis, and if the diagnosis of contracted pelvis were always confirmed, as it should be, by X-ray pelvimentry, and if inductions were not done till the end of the 37th week we are of opinion that the results from induction might compare favourably with those from trial labour and the Caesarean section rate be considerably lower.

The section on external prophylactic version is excellent and the illustrations of this operation are the best that we have seen. In Cardiff the version is not attempted till 36 weeks which we think is 2 or 3 weeks too late. The importance of obtaining an X-ray picture before attempting it is rightly emphasized but no mention is made of the advisability and indeed the necessity for accurate X-ray pelvimetry if the attempt at version fails and we are faced with a breech delivery, for as is pointed out a breech delivery through a contracted pelvis can be an exceedingly hazardous enterprise. The statement is made that if, in a breech delivery, the cord is not pulsating after the breech is born, the foetus is dead. This is not by any means always so. Neither can we agree with the advice given in the section on fibromyomata in pregnancy that, where Caesarean section is necessary, myomectomy should be done at the same time as the section. The safety of the patient will be best ensured by postponing the myomectomy till some time later, when it can be done with far less risk of shock.

There is an excellent section on postnatal examination, but it is surprising to find that cervical erosion in the postnatal patient is treated by application of mercurochrome "thrice and later twice weekly for about 6 weeks," when the erosion can be cured at one sitting by radial cauterization by the electric cautery! It is, however, a pleasure to quote Professor Strachan's opinion on the treatment of postnatal retroversion. "In our view far too much attention has been paid to retroversion and it is questionable if a simple mobile retroversion uncomplicated by inflammatory adhesions produces any symptoms . . . We have met many more women who have become neurotic and introspective simply by being told, possibly many years previously that they had a displaced womb." With this statement we most heartily agree for we believe that in the past the treatment of retroversion and playing about

with pessaries for its "cure" has bulked far too largely in the routine of the postnatal clinic.

Finally, two aphorisms are worth quoting: "When a fibroid is present along with pregnancy it is the pregnancy that is apt to be overlooked, but when an ovarian cyst complicates pregnancy it is the cyst that is likely to be missed." And again: "The longer things are left to nature the less there is for the obstetrician to do." Dr. Arthur Watkins has contributed a valuable section on "The Care and Disorders of the Newborn Child", and Dr. Drummond, Transfusion Officer to the Welsh Board of Health, a very readable one on "Blood Transfusion in Obstetrical Practice." These add materially to the value of a very valuable book.

F. J. BROWNE

Expansion of Health Services in Kashmir

THE recent expansion of the Health Services of Kashmir provides medical facilities for even the most remote areas. The eighty-eight new rural dispensaries opened in 1947 provide beds for indoor patients, as well as other medical services. For every ten rural dispensaries there is a central dispensary with a large number of beds, equipped for surgical and medical treatment. These rural dispensaries also function as rural health centres and attend to sanitation, water supply, vaccination, maternity and child-welfare, nutrition, school health and the prevention of epidemics.

Three well-equipped and up-to-date hospitals were recently constructed at Srinagar, Jammu and Mirpur, provided with modern equipment and specialists who have trained outside India. These institutions serve also as training centres; those at Jammu and Srinagar have 500 beds. The opening of a Medical College in the State is contemplated.

Great progress has been made in preventive medicine. Vaccination is compulsory, and the incidence of deaths from small-pox and cholera is negligible. No cases of plague have occurred since 1938, and an Infectious Diseases hospital will shortly be opened at Srinagar.

At Tangamarg, one of the most beautiful health resorts, a well-equipped sanatorium accommodates 100 patients, and in order to segregate patients more completely the Tuberculosis Hospital at Srinagar is being expanded to accommodate 100 patients also. Expansion of the T. B. Hospital at Jammu is being undertaken.

REVIEW OF CURRENT LITERATURE

The Journal is fortunate in being able to run this Review in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Review will, however, contain in addition abstracts of articles which, though not of sufficient general interest for publication in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.1. There is special need of abstracters in foreign languages, and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstracter will be acknowledged in the text and payment will be made at the rate of thirty shillings per thousand words.

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ANATOMY

364. **A Spiral Artery in the Ovary of the Rabbit.** By S. R. M. REYNOLDS. *Amer. J. Obstet. Gynec.*, **53**, 221–225, Feb. 1947. 6 figs., 3 refs.

365. **Standardized Radiological Pelvimetry. 1. Quantitative Aspects.** By E. P. ALLEN. *Brit. J. Radiol.*, **20**, 45–54, Feb. 1947. 5 figs., 22 refs.

After discussing the lack of uniformity in the various methods of radiological pelvimetry the author suggests a series of 6 requirements for a standard system. (1) All significant diameters must be measured with sufficient accuracy for practical purposes. (2) The method must be capable of application to all standard apparatus. (3) Accurate description must be possible so that other workers can follow the method. (4) It should be simple and avoid complicated mathematics. (5) It should provide some basis for morphological classification of the pelvis. (6) It should be sufficiently concise to permit application by those without great experience.

The author bases his arguments and observations on the examination of 220 primigravidae and upon the results of mensuration of 12 dried pelves. The latter are all specimens of 50 years ago and 10 of them are from Maori natives. He does not suggest that the latter are fully representative of the skeleton of to-day, but he uses the results of his measurements to make certain points later in the paper. He states that it is the function of pelvimetry to investigate the clinically inaccessible lower parts of the pelvis rather than the brim, for which the foetal head remains the best pelvimeter. In discussing actual mensuration he makes a plea for accuracy and for the abandonment of those measurements relying on the identification of external bony points. With regard to the transverse measurements, he points out that all the usual ones have well-defined bony end-points, except the bituberous and the anterior transverse, and that the oblique diameters are of doubtful value if the conjugate and the transverse are known. With regard to the measurement of the true conjugate he suggests that most information can be obtained from this measurement by altering its posterior end-point according to the size of the pubosacral angle—that is, the angle formed between the classical conjugate and the plane of the anterior surface of the first sacral vertebra. Where this angle is less than 90 degrees the smallest available diameter lies below the classical conjugate and is approximately the conjugate of Caldwell and Moloy; where it is more than 90 degrees the classical conjugate gives the available diameter. In the author's experience the majority of pelves have a pubosacral angle of 90 degrees or more.

In the midplane he suggests the addition of a fourth measurement to the usual three—namely, the anterior or true transverse (between the flat opposing surfaces of the ischia anterior to the bases of the spinous processes). Although the fourth sacral segment is taken as the posterior end-point of the sagittal diameter in this plane, the more reliable end-point is the tip of the last fixed sacral segment. While the bispinous diameter is nearly always employed as the significant diameter in the mid-plane, most of the cases examined had 64 per cent of the sagittal diameter in this plane in front of the bispinous diameter, so that the available bony diameter is greater than the bispinous measurement would suggest and the head would pass easily anterior to the spines. This available diameter can be assessed by making a graphic reconstruction of the midplane at this level and then finding the anterior transverse diameter.

For the outlet he recommends the measurement of the subpubic angle by the method of Chassard and Lapine, of the bituberous diameter, and of the pubotuberous diameter. He considers the posterior sagittal of Klein to be too unreliable and too difficult to measure accurately. Of the measurements in this plane, the only one which can be made accurately is the subpubic angle, but this alone does not give full information as to the size of the outlet, and the author suggests that a further advance can be made by measuring the symphysis-biparietal distance. Two subsidiary methods of assistance are suggested, that of charting or reconstruction and that of calculation of the areas of the inlet and midplane. *P. J. Kerley*

366. **Standardised Radiological Pelvimetry. II. Qualitative.** By E. P. ALLEN. *Brit. J. Radiol.*, **20**, 108–118, Mar. 1947. 2 figs., 23 refs.

367. **Graphic Portrayal of Relative Pelvic Size.**
By W. F. MENGERT and W. C. ELLER. *Amer. J. Obstet. Gynec.*, **52**, 1032–1040, Dec., 1946. 4 figs., 3 refs.

The authors consider that the methods in common use for estimating the pelvic capacity do not give a clear mental picture of the pelvis. They recommend that the approximate size and shape of the inlet, mid-pelvic, and outlet planes should be plotted on a sheet of paper on which is a graphic outline of their normal counterpart. The probable course of labour in mild degrees of disproportion can be more readily foretold if, in addition, a diagrammatic, transparent, plastic " cut-out " of small, average, and large foetal heads is superimposed on the graphic outline of the pelvic size.

Gladys Dodds

368. **Recognition of Midpelvic Contraction.**
By W. C. ELLER and W. F. MENGERT. *Amer. J. Obstet. Gynec.*, **53**, 252–258, Feb., 1947. 5 figs., 11 refs.

In the past much attention has been paid to the anatomy and measurements of the pelvic inlet and outlet. The authors of this paper, writing from the Department of Obstetrics and Gynecology, Southwestern Medical College, Dallas, feel that not enough interest has yet been aroused in configuration of the midpelvic plane. Abnormalities of this plane may not infrequently account for difficult labour and for stillbirth, and lead to dangerous operations on the foetus. A plea is put forward for the study of this plane and for its more frequent estimation by radiological methods. Only when clinics have done this in more cases will it be possible to assess the frequency of mid-plane contraction and to analyze the effects on labour.

Kenneth Bowes

PHYSIOLOGY

369. **Sensory Innervation of the Adnexa and Uterus.** (La innervazione sensitiva utero-annessiale. Contributo alla fisiologia del sistema nervose vegatitivo nell' uomo.)

By G. PIERI. *Clin. ostet. ginec.*, **49**, 1–21, Jan.-Feb., 1947. 4 figs., 20 refs.

370. **Ovulation without the Formation of a Corpus Luteum in the Human Subject.** (Ovulation ohne Corpus luteum-Bildung beim Menschen.)

By H. STIEVE. *Med. Klinik.*, **41**, 479-482, Oct., 1946. 11 refs.

The author describes the changes in the ovarian follicle during its development and after its rupture. He believes that the granulosa cells multiply considerably before the follicle ruptures, and that immediately after the ovum is extruded vascularization occurs, the granulosa cells enlarge, and the corpus luteum is formed. As a result of secretion of the corpus luteum the endometrium undergoes changes which prepare it for the reception of the ovum.

He has on rare occasions observed cases where after the follicle has ruptured, a corpus luteum has not formed. One such case occurred in a nulliparous woman, 32 years old, who died suddenly as the result of an accident. She had menstruated for 4 to 6 days every 24 to 32 days. Her last menstrual period was on December 5th, 1943, and she died on December 29th, 1943. Postmortem examination showed a healthy woman with no signs of disease. The genital organs were normal. The endometrium was in the proliferative phase about the fourteenth to eighteenth day of the cycle. The right ovary contained numerous follicles at various stages of development and a 6-weeks-old corpus luteum of menstruation. The left ovary also had numerous follicles and a projecting dark-red mass with a small opening on the surface closed with fibrin. This mass measured 10 × 6 mm. and it was filled with coagulated blood and fluid. The inner wall of this consisted of a layer of numerous fibrocytes and collagen substance. The fibrocytes were 6 to 8 mm. long and lay either singly or in groups. Numerous mitotic figures were present. Towards the centre, around the coagulated blood, the cells were proportionately filled with a dark-brown substance. There were no ovum and no granulosa cells in the mass.

The microscopical findings resemble in some ways those seen with an atreptic follicle in which the granulosa cells have disappeared and the theca interna has reformed. The rupture point and the marked folding of the wall resemble rather a corpus luteum than an atreptic follicle. To such bodies the author gives the name " theca body " or " corpus fuscum ". The granulosa cells must all have been extruded with the ovum, corona radiata, and discus proligerus. The reason for this is not obvious, but the phenomenon is of clinical as well as scientific interest.

Gladys Dodds

371. **Regular Appearance of a Specific Proteinase during Menstruation.** (Ueber das regelmässige Auftreten einer spezifischen Proteinase während des mensuelen Zyklus.)

By H. ROEMER. *Klin. Wschr.*, **24–25**, 116–121, Nov. 15 and Dec. 1, 1946. 14 figs., 2 refs.

Becker-Glauch and Winkler demonstrated the presence of a specific proteolytic substance in the urine of women on certain days during the menstrual cycle. They used a modification of Abderhalden's test and estimated quantitatively the amount of the proteinase. At the Universitäts-Frauenklinik, Giessen, the author has carried these investigations one stage further by examining daily 24-hour specimens of urine during complete menstrual cycles. He has found proteinase regularly present at definite times: just before the onset and during menstruation, and about the middle of the menstrual cycle. In 2 cases the proteinase occurred on two separate occasions during the intermenstrual period. In the remaining days of the cycle the proteinase was absent.

The time of appearance of the proteinase does not correspond with the secretory curves of the follicular or of corpus luteum hormones. The author postulates, since the proteinase is present at the middle of the menstrual cycle at the normal time of follicle rupture, either a specific ovum hormone or that the breakdown of cells discharged from the rupture of the follicle produces this specific protein. The presence of the proteinase on two occasions during the intermenstrual period would suggest that ovulation had occurred twice in that cycle. The author suggests that, as the proteinase is regularly excreted always just before or with the onset of menstrual bleeding, either it is produced by a hormone set free from the dead ovum or the hormone from the degenerating corpus luteum contains the same proteinase as that of the ruptured follicle.

This report is a preliminary one and further work is being done on the urine of pregnant and menopausal women. The demonstration of the regular physiological appearance of this specific proteinase during the menstrual cycle opens up another avenue of investigation on the cyclic hormonal control of menstruation.

G. Dodds

372. **Cyclic Changes in the Physical and Chemical Properties of Cervical Mucus.**

By W. T. POMMERENKE. *Amer. J. Obstet. Gynec.*, **52**, 1023–1031, Dec., 1946. 1 fig., 24 refs.

Observations were made on cervical mucus throughout the menstrual cycle, except during menstruation. The mucus was obtained by aspiration from the external os and the cervical canal. The subjects investigated were young women with normal cycles and normal pelvic findings.

The maximal production of mucus occurred during the ovulatory phase, when it was 10 to 12 times the amount at other phases. The viscosity of the mucus was found to be so low in this phase that it could traverse a given distance through a capillary tube in only 2 to 3 seconds, while mucus obtained at other phases took 100 seconds to traverse the same distance under the same set of standard experimental conditions. During the ovulatory phase also, spermatozoa penetrated the mucus readily and rapidly at a rate of 3 mm. per minute, while the rate was 0.25 mm. at other phases. The water content of cervical mucus was highest in the ovulatory phase. Chemical investigations showed variations in the amount of carbohydrate and amino-acids in the mucus during the cycle. These observations suggest that the cervical mucus during ovulatory phase is the most propitious for the reception, passage, and nutrition of spermatozoa.

Gladys Dodds

PREGNANCY

Normal.

373. **Biological Titration of Gonadotrophins in Obstetrics.** (Titulación biológica de las gonadotropinas en obstetricia. [Trabajo de ingreso.])

By G. VILLAVICENCIO. *Bol. Soc. chil. Obstet. Ginec.*, **11**, 166–183, Oct., 1946. 13 refs.

374. **Estimation of Oestrone in the Urine in Pregnancy.** (Le dosage de l'oestrone urinaire au cours de la grossesse.)

By C. MAYER. *Rev. franc. Gynéc.*, **41**, 337–346, Nov., 1946. 27 refs.

Oestrogens are substances capable of causing keratinization of the vagina and oestrus in the castrated female rat or mouse. The basic substance is oestradiol ($C_{18}H_{22}O_2$), formed in the

ovaries. In human urine two derivatives are found: oestrone ($C_{18}H_{24}O_2$) and oestriol ($C_{18}H_{24}O_3$). The oestrogenic activity of human urine is due almost entirely to oestrone, as oestriol has only 0.9 per cent of the activity of oestrone, while oestradiol is present in negligible quantities only. There are two methods of estimating oestrone—the biological and the colorimetric. The biological method may determine either the keratinization of the vagina (as shown by the examination of vaginal smears) in the castrated rat or mouse, or the size of the introitus in the immature rat, or the increase in weight of the uterus of the immature rat or mouse. All these tests are complicated in interpretation, need a large number of animals, take 24 hours or longer, and are subject to an error of 20 per cent. The units used are also considered unsatisfactory. The colorimetric method is based on the development of a pink colour when β-naphthosulphuric acid is added to oestrone, the depth of the colour depending on the amount of oestrone (Kober's reaction). As this colour disappears on addition of hydrogen peroxide, the estimation in the urine entails a comparison of the final residual colour with a standard. The method is comparatively rapid and easy and is more accurate than the biological one. During pregnancy the amount of oestrone in the urine increases, the actual level depending on the size of the placenta. The author regrets that estimations of oestrone are not universally measured in μg. of oestrone but in rat and mouse units, the relation between the various units being: 1 mouse unit equals 8 international units; 1 rat unit equals 32 international units; 1 international unit equals one-tenth μg. He concludes this interesting article by describing his own method of preparing the urine for a colorimetric examination and by giving in detail the results in 10 cases of pregnancy on which altogether 72 estimations were performed; in 2 cases the first estimation was done as early as 6 weeks after the beginning of pregnancy, and in 7 cases the final estimation was made after labour (there being a dramatic drop in the level after delivery). In one of the cases at 3 months the amount was 620 μg. per 1,000 ml., and at 4 months only 450μg. per 1,000 ml., a miscarriage occurring 2 days after this last estimation.

Nicholas Tereshchenko

375. **The Value of Plasma Pitocinase Determinations in Obstetrics.**

By E. W. Page. *Amer. J. Obstet. Gynec.*, **52**, 1014–1022, Dec., 1946. 3 figs., 19 refs.

A series of cases is recorded in which quantitative estimations have been made of an enzyme present in the blood. This enzyme destroys the oxytocic properties of pitocin and is referred to as pitocinase. From the fourth to the sixteenth week of normal pregnancy there is a 100 per cent increase in plasma pitocinase every 12 days. By quantitative estimation during this time the date of conception can be calculated to within 6 days. From the sixteenth to the thirty-eighth week there is a further increase of pitocinase, but the rate of increase is less steep than in the early weeks, so that the time of conception or of delivery cannot be accurately estimated. Pitocinase remains at a high level in the blood during labour. After delivery it decreases and disappears in 4 weeks. Twins, triplets, and intrauterine death do not alter the quantitative values from the normal range. The placenta at term has 30 to 50 units of pitocinase per gramme of tissue. The enzyme is not present in the foetal blood. Quantitative estimations were made in 16 pre-eclamptic and eclamptic patients and no correlation was found between the amount of pitocinase and the severity of the disease. Traces of pitocinase were found in 20 non-pregnant patients. Packed red cells, after haemolysis, contained the same amounts per gramme of the enzyme as did plasma at full term, regardless of species or sex.

Gladys Dodds

376. **Investigations into the Tocopherol Content of the Blood of Pregnant and Aborting Women.** (Undersogelser over Tokoferolindholdet i Blod. En Sammenligning mellem Tokoferolindholdet i Blodet hos gravide og aborterende Kvinder.)

By K. Faaborg-Andersen. *Nord. Med.*, **42**, 2401–2404, Oct. 18, 1946. 47 refs.

A non-specific chemical method was used to study the level of vitamin E in the blood of 25 healthy pregnant women and 48 women who had aborted. The range found was 1.9 to 17.2 μg. per ml. for the healthy and 1.6 to 17.6 μg. per ml. for the patients who had aborted. There is no detectable difference between these ranges.

G. Discombe

377. **Placental Toxin: Inactivation and Tolerance during Pregnancy.**

By C. L. SCHNEIDER. *Amer. J. Physiol.*, **147**, 255–259, Oct., 1946. 3 figs., 6 refs.

Blood contains an inactivator for a placental toxin. The present paper shows that the potency of the inactivator rises during pregnancy both in mouse and man.

Extracts of fresh placenta were used as reagents for the measurement of the inactivator. The frozen extracts were thawed, centrifuged, assayed, and diluted to appropriate concentrations. The toxic extracts used as reagents were prepared from dry placental powder; mixtures of toxic extract of pH 7.4 and different amounts of diluted serum and sufficient saline to yield an initial toxin content of 20 units per ml. were prepared, the serum being added last in each case. The inactivating potency in units was that dilution determined by interpolation which caused 50 per cent inactivation of the toxic extract.

The inactivator in the serum has the properties of a protein. The increase in titre began in human pregnancy after the tenth week, the maximum titre being reached just before term. Normal levels were restored a few weeks after delivery. In mice the maximum titre was also reached before term and averaged approximately 2½ times the normal. At the same time, and in spite of the greater inactivating potency of the serum, sensitivity to the toxic extracts increased about 2½ to 4 times during pregnancy. In contrast with non-pregnant mice, liver necrosis was encountered only rarely in pregnant mice after sub-lethal doses of toxin. The pregnant mice were not easily desensitized. However, with careful repetition and increase of dose a desensitization or refractory period could be induced. Then massive doses (20 to 40 units) given during the refractory period regularly resulted in focal liver necrosis. This response was the same as that obtained from non-pregnant mice after they had received massive doses during the refractory period, which could be induced readily by single sub-lethal doses of toxin. After treatment with massive doses the pregnant mice, like the non-pregnant ones, besides the focal liver necrosis, occasionally had blood in the small intestine, and some developed bilateral cortical kidney lesions. The foetuses were usually dead at sacrifice if the animals had not already been aborted.

F. J. Browne

378. **Desensitization of Mice to Placental Toxin.**

By C. L. SCHNEIDER, *Amer. J. Physiol.*, **147**, 250–254, Oct. 1946. 5 figs., 3 refs.

The placental toxin is a protein, inactivated by heating to 85°C. for 10 minutes, poorly soluble in water, and precipitated by half-saturated ammonium sulphate solution or 15 per cent alcohol in the cold. In the simple saline extracts 0.10 mg. of protein corresponded to 1 unit of toxin; for preparations reprecipitated with alcohol 0.06 mg. corresponded to 1 unit. Intravenous injections were lethal to mice while sub-lethal doses resulted in focal liver necrosis. After these single intravenous injections the sensitivity of the mice decreased. The onset of the desensitization was rapid, and in 3 minutes after the injection the mice were able to survive 7 units (7 M.L.D.); within 10 minutes they could survive more than 20 M.L.D. —that is, enough to kill more than 20 untreated mice. Within 24 hours the sensitivity had returned almost to normal. There were visible focal liver lesions in 95 per cent of the animals desensitized and afterwards treated by massive doses of toxin. Bleeding into the small intestine was not uncommon and the kidneys showed toxic changes.

F. J. Browne

379. **The Kidneys and Pregnancy.** (Nier en zwangerschap.)

By M. A. van BOUWDIJK BASTIAANSE. *Belg. Tijdschr. Geneesk.*, **3**, 193-207, Mar. 1947.

380. **The Importance of the Liver in Reproductive Physiology.**

By S. J. GLASS. *West. J. Surg.*, **55**, 114–119, Feb. 1947. 17 refs.

381. **Experimental Study of the Passage of Sulphonamides from the Blood Serum of the Mother to that of the Foetus in the Amniotic Liquid and in the Lochia.** (Contributo sperimentale allo studio del passaggio dei sulfamidici dal sangue della madre nel sangue fetale, nel liquido amniotico e nei lochi.)

By A. CARIANNI. *Ginecologia, Torino*, **13**, 37-46, Jan. 1947. 5 refs.

382. **The Laboratory Diagnosis of Pregnancy.**

By J. BAMFORTH. *Practitioner*, **158**, 154–157, Feb. 1947. 16 refs.

383. **The Hogben Test in Comparison with the Determination of Chorionic Gonadotrophin by Weight in Early and Interrupted Pregnancy.** (Hogbentest im Vergleich mit der gewichtsmässigen Choriongonadotropinbestimmung bei Früh-und gestörter Gravidität.)

By C. A. JOEL. *Schweiz. med. Wschr.*, **76** 1106–1107, Oct. 26, 1946. 1 fig., 3 refs.

The results of the Hogben test, in which the clawed toad, *Xenopus laevis*, is used for the diagnosis of early pregnancy, have been compared with the results of the Aschheim-Zondek reaction and with the results of estimation of chorionic gonadotrophin by weight in the urine. Tests have been performed in early and in interrupted pregnancy. It was found that at the sixth week of pregnancy the Hogben test was still negative; it should not, therefore, be used for the diagnosis of very early pregnancy. By the seventh or eighth week the results with the Hogben test are similar to those obtained by the other two methods. In interrupted pregnancy a parallel fall in chorionic gonadotrophin excretion and in reaction to the Hogben test takes place. *Josephine Barnes*

384. **An Evaluation of the Pregnancy Test Based on Ovarian Hyperemia in the Immature Rat.**

By C. A. BUNDE. *Amer. J. Obstet. Gynec.*, **53**, 317–320, Feb. 1947. 6 refs.

385. **Further Observations on the Two-hour Pregnancy Test.**

By H. S. KUPPERMAN and R. B. GREENBLATT. *J. med. Ass. Georgia*, **36**, 58–63, Feb. 1947. 22 refs.

386. **Nutrition in Pregnancy. The Effects of Dietary Deficiency in Pregnancy and the Detection and Treatment of Nutritional Deficiency Diseases.**

By C. F. VILTER, D. MORGAN, and T. D. SPIES. *Surg. Gynec. Obstet.*, **83**, 561–571, Nov. 1946. 3 figs., 64 refs.

Nutritional failure is more likely to occur during the course of pregnancy and lactation than at any other period of a woman's life. Strangely enough there has been no demonstration that malnutrition has anything to do with conception in women. The same factors that operate to induce nutritional failure in any person are applicable in pregnancy —namely: (*a*) failure of ingestion of foodstuffs, (*b*) increased requirements, (*c*) interference with absorption, (*d*) interference with utilization, (*e*) increased excretion, and (*f*) increased destruction. The first two account for most of the nutritional trouble in pregnancy.

*Recommended Daily Allowances of Specific Nutrients for the Non-Pregnant, Pregnant, and Lactating Women.**

Nutrients	Non-Pregnant	Pregnant (latter period)	Lactating
Calories	2500	2500	3000
Protein (g.) ...	60	85	100
Calcium (mg.)	0.8	1.5	2.0
Iron (mg.)	12	15	15
Vitamin A (I.U.)	5000	6000	8000
Thiamine (mg.)	1.5	1.8	2.3
Ascorbic acid (mg.)	70	100	150
Riboflavin (mg.)	2.2	2.5	3.0
Nicotinic acid (mg.)	15	18	23
Vitamin D (I.U.)	+	400–800	400–800

* Food and Nutrition Board, National Research Council, Reprint and Circular Series No. 115, 1941.

The factors predisposing to nutritional disease in the mother are the parasitic demands of the foetus, the economic status (availability does not insure an adequate dietary), nausea and vomiting of the first trimester, and multiple pregnancy. A study of 229 mothers between 18 and 45 years old at the Nutrition Clinic in Birmingham, Alabama, was made, disease symptoms being correlated with age, the time of their appearance, and the number of pregnancies. Only 4 out of 229 mothers had definite symptoms of nutritional disease before the first pregnancy, but 135 developed symptoms during lactation or pregnancy. The onset of symptoms was mostly in the third trimester, and commonest during fourth and fifth pregnancies. The mother is likely to give the food of higher quality to her husband and children, and the allotment of food for the family remains unchanged during her pregnancy. Isolated syndromes such as anaemia pellagra or neuritis are always a manifestation of a general and mixed nutritional deficiency. Treatment of the single symptom with a single specific substance without dietary control and combined therapy results in incomplete recovery.

Beriberi (polyneuritis of pregnancy) often follows

hyperemesis gravidarum and hence may appear early in pregnancy. Synthetic thiamine in doses of 5 to 20 mg. daily ameliorates the disorder. Macrocytic anaemia of pregnancy shows occasional refractoriness to parenteral treatment with liver preparations. Synthetic folic acid has recently proved effective in all varieties of macrocytic anaemia due to deficiency of liver principle, not excepting the macrocytic anaemia of pregnancy. Whether given orally or parenterally, and adequate daily dose (approximately 10 mg.) is followed by the appearance of reticulocytes in the peripheral blood and restoration of blood counts to normal. This is a rare dyscrasia in the United States.

Niacin deficiency causes in the pregnant woman the same signs and symptoms of pellagra that are found under circumstances unrelated to reproduction. There is a possibility that prenatal and postpartum psychoses might be related to deficiency of vitamin-B complex. Warkany has shown that deficiency of riboflavin during the differentiation stage of the rat embryo produced congenital abnormalities, such as " shortening or absence of ribs, digits, and extremities, shortening of the mandible, cleft palate, deformities of the eyes, and similar anomalies ". It is also responsible for angular stomatitis. Deficiency of vitamins C and K is briefly discussed. Congenital blindness is induced by vitamin-A deficiency in the calf, pig, and rat. As regards vitamin-D deficiency, it is a physiological impossibility to drain calcium from the erupted tooth, so pregnancy does not aggravate or initiate dental caries. Vitamin E is only very briefly mentioned. The causes of the anaemia are iron deficiency and chronic blood loss.

The maintenance of an adequate protein intake is a major factor in directing an efficient pregnancy. Protein deficiency, if not the initiating cause of toxaemia, is a prominent predisposing factor. The view that high protein intake induces toxaemia has given way to the view that the very opposite is true. Some investigators still believe that there is no correlation between the amount of dietary protein and toxaemia, but it is reasonably safe to say that the woman whose protein intake during pregnancy has been adequate usually does not develop toxaemia. Such a dietary includes a quart of milk, two moderate servings of meat, and one to two eggs, daily. A good supply of protein during pregnancy also ensures the best conditions for successful lactation.

The principles of treatment advised for nutritional disease occurring during pregnancy do not differ from those prescribed in non-pregnant women—namely, (*a*) a diet providing 3,500 to 4,000 calories, including 120 to 150 g. protein, adequate vitamins, and minerals; (*b*) synthetic vitamins in balanced amounts; (*c*) specific therapy with synthetic vitamins directed at the more prominent symptoms; and (*d*) a natural source of vitamin-B complex, such as brewers' yeast, crude liver extract, or wheat germ.

[In many European countries this article will have to be laid aside and resurrected when rationing ends. The apparent increase in intrauterine death of the foetus and of cases of toxaemia may have something to do with the long period of rationing in Britain, and, from this point of view, the opinions expressed in this paper are interesting.] *G. Gordon Lennon*

Abnormal.

387. **The Value of the Alkali Reserve Test in Obstetrics and Gynecology.**

By A. Sadovsky and R. M. Heifetz. *Exp. Med. Surg.*, **4**, 306–309, Nov. 1946. 2 refs.

Tissue anoxia due to accumulation of carbon dioxide is normally prevented by the buffer system of the blood and the alkali reserve. Diminution in the alkali reserve may be met with in vomiting of pregnancy, eclampsia and pre-eclampsia, labour (especially if prolonged), and general anaesthesia. The combination of general anaesthesia and obstetric complications may be very dangerous. Alkali reserve estimations (224) were made by the Van Slyke method in 147 cases of various obstetric complications of labour and, for comparison, in gynaecological operations (96 gynaecological cases, 18 cases of pregnancy, and 35 deliveries). In the gynaecological group only a few patients had a low reserve before operation, and in these cases operation was deferred. Ether was found to aggravate acidosis, whereas local analgesia did not. The authors therefore stress the value of the latter. The alkali reserve was lowered even in normal labour, and more markedly so if labour was prolonged. Out of 69 examinations made during delivery 34 gave values below 40 volumes per cent. In eclampsia the value fell to 28.1 volumes per

cent the day before fits and to 17.6 volumes per cent during fits. In jaundice the value was 26.6 volumes per cent. Diminution was also observed in cardiac disease complicating pregnancy.

R. K. Bowes

388. **Eclampsia. Report of a Case in which there was Extensive Destruction of the Brain.**

By H. JOSEPHY and E. F. HIRSCH. *Arch. Path., Chicago*, **42**, 391–401, Oct. 1946. 4 figs., 13 refs.

A case of post-eclamptic cerebral atrophy in a white girl aged 15 years is described. Only one other case was found in the literature. Pre-eclampsia with its usual signs appeared at the eighth month of pregnancy and progressed until labour was induced medically. During labour the patient had 5 generalized convulsions, and after delivery she passed into a condition resembling status epilepticus for 45 minutes until "sodium amytal" was administered. Subsequent convulsions were similarly controlled. Eleven days after induction of labour a condition resembling decerebrate rigidity developed and persisted until the patient died 3 months later without regaining mental consciousness. The temperature varied between 101° and 104°F. (38.3° and 40°C.). A ventricolugram demonstrated the presence of cerebral atrophy. The essential finding at necropsy was the presence of flat atrophic convolutions with narrow sulci affecting more specially the frontal, temporal, and anterior part of the parietal regions. Coronal section of the cerebrum after formalin fixation showed narrowing of the cortex, which was separated from the centrum ovale by a layer of soft loose tissue. In some places the cortex was actually separated from the white matter. The latter was pale and friable, these changes being most marked in the temporal poles. The lateral ventricles were dilated but otherwise the brim was normal. Blocks of tissue were embedded and stained with toluidine blue, by van Gieson's method, and for myelin sheaths, neurofibrils, mesenchymal structures, and lipids. A detailed description of the histological changes is given, the salient points being extensive demyelination of the parietal lobe and the second and third temporal gyri, together with destruction of the cortex of the anterior parts of the cerebrum and especially the first and second frontal gyri. In the cortical lesions there was marked loss of nerve cells and fibres, the subsequent reactions being either softening with organization, or gliosis. The blood vessels were dilated and small haemorrhages were found. The basal ganglia and brain stem were normal. In the cerebellum, Purkinje cells and the cells of the dentate nucleus were considerably reduced in number.

The authors summarize their findings and point out that they observed the early stages of what was described by Lowenberg and Lossman in their case (the only other one on record), in which death occurred 7 years after the eclampsia. They review numerous reports of other less severe changes and, comparing them with their own, form the opinion that the pathogenesis of all these changes is essentially vascular, involving vasoparalysis and thrombosis of capillaries and venules. They admit that a toxic factor such as anoxaemia may be partially responsible for the demyelination of the centrum ovale.

R. B. T. Baldwin

389. **Late Postpartum Eclampsia.**

By H. J. STANDER, R. W. BONSNES, and W. B. STROMME. *Amer. J. Obstet. Gynec.*, **52**, 765–772, Nov. 1946. 5 figs., 1 ref.

In the light of their previous experience the authors held the view that in the majority of cases postpartum eclampsia occurred within 72 hours of delivery. They have had to modify their view, however, on account of recent experience to include the first week of the puerperium. During the period from September 1st, 1932, to January 1st, 1946, there were 70 cases of eclampsia in the New York Lying-in Hospital, and of these the eclampsia occurred postpartum in 23 cases. In all but 3 of these it took place within 30 hours of delivery. The 3 late cases in which there was postpartum eclampsia respectively on the fourth, sixth, and eighth days after delivery, are recorded with full details of the clinical findings and laboratory investigations. All 3 showed the features characteristic of true eclampsia—namely hypertension, albuminuria, oedema, convulsions, elevated uric acid level and decreased carbon-dioxide combining power in the blood, decreased uric acid clearance and diminished urinary output. There was a return to normal after the eclampsia in all but one patient, who had a persistent hypertension.

T. N. MacGregor

390. **Prognostic Significance of the Diastolic Blood Pressure in Eclampsia Patients.** (Die prognostische Bedeutung des diastolischen Blutdruckes der Eklampsiekranken.)

By L. VACZY. *Gynaecologia*, **122**, 244–251, Oct. 1946. 22 refs.

It is difficult to decide whether the course of an eclamptic case will be mild or severe. Various investigations, such as estimation of the histamine content of the urine, measurement of capillary pressure in the skin or of muscle tone, and liver function tests, have been suggested in the past but are of little use at the bedside. They require a laboratory and good technicians, and several hours must elapse before a result can be obtained. This paper shows the value of blood-pressure readings in the prognosis during the acute stage of eclampsia. The systolic, pulse, and diastolic pressure readings in 24 cases are discussed.

No prognostic significance could be attached to the systolic blood-pressure. Thus, 12 of the 24 patients had an average systolic blood-pressure of over 100 mm. Hg. and had only 3 fits, while 12 patients with an average systolic pressure of 178 mm. Hg. had more than 3 fits. Further, 7 women who had only 1 fit had a systolic pressure of over 200 mm. Hg., while 6 women who had 5 fits had a systolic pressure of less than 200 mm. Hg. The pulse pressure was also of no prognostic value. There appears to be some relation between the height of the diastolic blood-pressure and the severity of the condition. Patients with a diastolic pressure of over 100 mm. Hg. generally had more fits than those with a diastolic pressure below 100. There was no absolute connexion between the height of the diastolic pressure and the number of fits, but it could be said that when the diastolic pressure was below 100 mm. Hg. the prognosis was better than when it was above 100.

Gladys Dodds

391. **Prevention and Modern Treatment of Eclampsia.**

By R. NEWTON. *Med. Press.*, **217**, 255–257, Apr. 2, 1947. 10 refs.

392. **Principles of Treatment in Pre-eclampsia and Eclampsia.**

By J. R. WILLSON. *J. Kansas med. Soc.*, **37**, 553–556, Dec. 1946.

393. **Relation of the Fetus and Placenta to the Decline of Hypertension in Pregnant Rats.**

By E. W. PAGE. *Amer. J. Obstet. Gynec.*, **53**, 275–278, Feb. 1947. 1 fig., 19 refs.

394. **Endocrine Influences Upon the Blood-pressure of Normal and Hypertensive Rats.**

By E. W. PAGE and E. OGDEN. *Amer. J. Obstet. Gynec.*, **53**, 150–154, Jan. 1947. 18 refs.

395. **Hypertension in Pregnancy.** (Hypertensie en zwangerschap.)

By M. RENAER, *Belg. Tijdschr. Geneesk.*, **3**, 208–218, Mar. 1947.

396. **Premature Separation of the Placenta (102 Cases).** (Förtidig placentarlösning. Sammanställning av 102 fall.)

By L. IACOBAEUS. *Nord. Med.*, **32**, 2509-2512, Nov. 1, 1946. 30 refs.

An analysis is given of 102 cases of premature separation of the placenta occurring in 20,640 deliveries at the Gynaecological Clinic, Lund. The cases are grouped according to severity of symptoms; 22 were mild, 49 moderately severe, and 31 very severe or fulminating. It has been suggested that the condition tends to occur more frequently in the higher age-groups, but this was not so in the series under analysis. There was a higher proportion of severe or fulminating cases among multiparae. Only 54 per cent showed albuminuria or other evidence of renal lesion, while only 12 of the patients had had a previous abortion. Nearly 60 per cent of the cases occurred at full term and 30 per cent in the ninth month. One case was definitely precipitated by attempted version for a foetal malposition.

Mild cases need no special treatment. In more severe cases delivery must be effected either naturally by forceps, or by vaginal or abdominal Caesarean section. Suitable adjuncts such as blood transfusion are used as indicated. The severity of symptoms and general condition of the patient determine the need for intervention, and no rule can be laid down for any given case. There were 9 vaginal and 17 abdominal Caesarean sections. Hysterectomy was not performed in any case. The maternal mortality was 2 per cent. Immediate foetal mortality—that is when the child was dead on arrival or died during delivery—was 53 per cent, but if the immediate postnatal period is included it was 63 per cent.

J. W. S. Lindahl

397. **Placenta Accreta Found at Caesarean Section for Placenta Previa, with Preservation of the Uterus.**
By W. F. SHANNON and C. F. DODENHOFF. *Amer. J. Obstet. Gynec.*, **53**, 326–328, Feb. 1947. 7 refs.

398. **Obstetric Hemorrhage, Incidence and Management. A Two-year Study (July 1, 1943, to July 1, 1945.)**
By W. R. PAYNE. *Sth. med. J.*, **40**, 161–166 Feb. 1947.

399. **Ten Years' Statistics of Abortion.** (Et 10-aars abortmateriale.)
By T. KAERN. *Ugeskr. Læg.*, **109**, 169–173, Feb. 13, 1947. 3 figs., 12 refs.

An analysis is made of 3,007 cases of abortion admitted to the St. Joseph Hospital, Copenhagen, between 1935 and 1945. Of these, 2,313 were early cases (up to the fourth month of pregnancy) and 694 late cases (fourth to seventh month of pregnancy inclusive). The abortion followed an afebrile course, in that the rectal temperature never reached 38°C., in 61 per cent of cases and a febrile course in 39 per cent. The mortality was 0.5 per cent and morbidity (conditions associated with the abortion) 28 per cent; the latter figure is is subdivided into 35 per cent of febrile cases and 23 per cent of afebrile cases. Active treatment was necessary in 87.1 per cent of all cases; 94.2 per cent of early cases were so treated but only 63.8 per cent of late cases

Aetiology is not discussed. The number of cases has increased steadily each year and has nearly trebled itself in the last decade. The proportion of abortions to live births is approximately the same for all age groups, but is greater in multigravidae. Approximately one-third of the patients were unmarried, and in these there was a slightly greater tendency to a pyrexial course. Of the 16 deaths, 10 were due to septicaemia (5 married, 5 unmarried), 4 to peritonitis (3 unmarried; 2 with a uterine perforation), 1 to peritonitis following an operation for salpingitis, and 1 to pulmonary embolism. The author thinks that between 80 and 90 per cent of the abortions had been induced.

S. S. B. Gilder

400. **The Obstetric Point of View in the Classification of Premature Births and Abortions.** (Obstetriska synpunkter beträffande nomenklaturen förtidsbörd abort.)
By C. VON NUMERS. *Nord. Med.*, **32**, 2745–2750, Nov. 29, 1946. 2 figs.

The limit between premature and mature birth weights is now generally fixed at 2,500 g., but a limit of foetal weight dividing premature birth from abortion has not been fixed. Henderson considered that a birth-weight of 1,250 g. should represent the lower limit for premature infants, and advocated the term pre-viable to describe infants with a lower birth-weight than this.

The present author discusses the results of his survey of the relation between birth-weight and chance of survival in a total of 2,642 infants, all of whom weighed under 2,500 g. at birth. The infants were classified in 19 groups with birth-weights from 600 g. to 2,500 g. In the lowest groups (600 to 900 g.) none of the 158 infants survived the first year of life. Ten of the 395 infants (28 per cent) in the next 5 groups (900 to 1,400 g.) were still alive after one year; and in the next group (1,400 to 1,500 g.) 13 out of 80 children (16.3 per cent) survived. In the group from 1,200 to 1,300 g., which includes Henderson's limiting value of 1,200 g., the average length at birth was 38.4 cm., and the average duration of pregnancy had been 206.7 days (29.5 weeks). The average weight of all infants born between the twenty-seventh and the thirtieth weeks of a pregnancy was 1,296 g. Thus the figure of 1,250 g. agrees fairly well with the old concept of viability in which a birth before the twenty-eighth week of pregnancy was considered to be an abortion.

After the author's paper it was officially decided by the Paediatric and Gynaecological Associations of Finland that for purposes of classification: (1) infants with a birth-weight between 1,250 g. and 2,500 g. will be referred to as premature; (2) infants with a birth-weight between 600 and 1,250 g. will form a special class and will probably be called immature infants; and (3) foetuses with a birth-weight below 600 g. will be considered to be the products of abortion.

S. S. B. Gilder

401. **A Study of the Pathology of Habitual Abortion.** [In English.]
By B. FALCONER. *Acta obstet. gynec. scand.*, **26**, 496–524, 1946. 8 refs.

The author analyzes 33 cases classed clinically as habitual abortion. Four cases were excluded from the discussion, as a normal pregnancy between a number of miscarriages had occurred in each.

Various causes were found to account for 14 of the remainder. Previous operation for ovarian cyst and fibromyomata accounted for 4. The presence of a uterus bicornis and a myoma was responsible for 2 more, and " tubal contractions " for another. Abnormal sperm counts were considered to point to the aetiological factor in a further 3. In the remaining 4 patients endometrial abnormalities were present: typical cystic glandular hyperplasia in 1, inactive tuberculous endometritis in 1, and dilated and cystic glands in a further 2. No evidence of an abortifacient element was found in the remaining 15 cases, and the author considers it reasonable to assume an immunobiological cause in some. He stressed the negative findings with regard to endometritis, but considers the presence of cystic glandular hyperplasia to be of particular interest.

[Defective spermatogenesis is a new observation in repeated miscarriages, and may well be the cause of " the blighted ovum ". But how it is to be treated?]

Braithwaite Rickford

402. **Fifteen Years Study of Abortion with Special Reference to Treatment.** (Et 15-ars abortmateriale —med saerlig henblikk pa behandlingen.)

By O. W. TENFJORD. *Nord. Med.*, **33**, 615–620, Mar. 7, 1947. 2 figs., 15 refs.

403. **Prevention and Treatment of Abortion.**

By L. M. JEFFRIES. *Med. Press.* **217**, 317-319, Apr. 16, 1947.

404. **A Simple and Rapid Method of " Approximate Dosage " of Gonadotrophic Hormones in Pregnancy.** (Su di metodo simplice e rapido di " dosaggio approssimato " delle gonadotropine gravidiche nella pratica clinica corrente.)

By A. MASCIO. *Clin. Ostet. Ginec.*, **48**, 225-234, Nov.–Dec., 1946.

The object of the present work is to discover a simple and rapid means of estimating approximately the quantity of gonadotrophic hormone in serum and urine, with especial reference to such pathological conditions as hydatidiform mole, chorion-epithelioma, and intrauterine death of the embryo. A modification of the Brindeau and Hinglais quantitative Friedman test is used. Only two test animals are generally necessary.

The condition of the test animal is important, and the author prefers to use rabbits about 3 months old and weighing 1,800 to 2,200 g. A preliminary laparotomy is performed to ascertain the state of the ovaries and to exclude any gross abnormality such as hermaphroditism. For the performance of the test it has been found that serum is to be preferred to urine. The use of urine has several disadvantages—excessive dilution of hormone, delay in the appearance of the reaction, toxicity of urine, and the possibility of non-specific positive reaction. Serum, on the other hand, can be collected at any time of the day, and the gonadotrophins are less labile; the content of gonadotrophin is similar to that in urine and more constant, hence it is better for quantitative determination. The unit of gonadotrophic activity is that proposed by Brindeau and Hinglais (U.B.H.) and is defined as " the least quantity of hormone which will, after one intravenous injection in a 2-kg. rabbit, produced within 48 hours a blood spot in one of the ovaries." The author quotes the paper by Brindeau and Hinglais, giving the significance of the quantitative estimations as follows. The presence of 750–1,500 U.B.H. per litre indicates a hypoactive placenta (tendency to abortion or intrauterine death). Fewer than 500 units indicates death of the embryo. A level of 1,500 to 25,000 U.B.H. occurs in pregnancy with normal placental activity and 25,000 to 50,000 U.B.H. in toxic pregnancy with normal embryonic development, as in hyperemesis gravidarum, and 60,000 U.B.H. or over in hydatidiform mole.

The author describes certain points from his own technique. He uses two animals and aims at establishing a " liminal positive reaction." In cases of suspected hydatidiform mole the serum is diluted to 1 in 30 and 1 ml. and 0.5 ml. are injected by the intravenous route. If both tests are negative, it is assumed that the serum contains under 30,000 U.B.H. per litre and the diagnosis of living hydatidiform mole is doubtful. Similar methods are applied to cases of threatened and missed abortion and to other pathological conditions associated with pregnancy. The method has proved of practical use and a valuable aid in diagnosis.

Josephine Barnes

405. **Placental Hormones after Death of Foetus with Viable Placenta.**

By B. ZONDEK. *Lancet*, **1**, 178–179, Feb. 1, 1947. 5 refs.

After expulsion of the placenta the pregnancy reaction of the urine normally remains positive for 8 days. When a positive pregnancy reaction becomes repeatedly negative it is proof that placental function has ceased, and the foetus is dead. But it is insufficient in diagnosing foetal death to rely on the negative result of only 1 pregnancy test, especially in the later months when the excretion of gonadotrophic hormone decreases and becomes less regular than in the early months. In the present paper the author presents evidence that the placenta can continue to excrete hormones for several weeks after the foetus has died and records 2 illustrative cases.

In the first case the patient was 8 months pregnant; foetal movements had ceased for 10 days when she was first seen on October 25th. No foetal heart sounds were heard and death of the foetus was diagnosed. Yet on November 12th the urine contained 10,000 rat units (R.U.) of follicle-stimulating hormones and 5,000 R.U. of luteinizing hormones per litre. On November 15th the amounts were respectively 1,000 and 500 R.U. A positive pregnancy reaction can generally be elicited with 1 or 2 ml. of urine—that is, with a gonadotrophin level of 500 R.U. per litre, so that 10 times this amount was present in this patient on November 12th. In the second case the foetus died in the eighth month. The serum-oestrone level was nevertheless high (500 mouse units per litre), thus suggesting that the foetus was alive. Three days later the patient expelled a foetus in such an advanced stage of maceration that it must have died 2 or 3 weeks earlier.

Spielman *et al.* had shown (*J. Amer. med. Ass.*, 1933, **101**, 266) that after extinction of placental function oestrogenic hormone disappears from the blood more rapidly than does gonadotrophin from the urine, and they therefore considered the disappearance of the oestrogenic hormone from the blood to be reliable evidence to foetal death. These cases demonstrate that even if the foetus dies the placenta can sometimes function normally and remain anatomically intact and in communication with the maternal circulation for as long as 4 weeks. In case 1 the placenta, analyzed for oestrogenic and gonadotrophic hormones, showed very low levels as compared with that of a living foetus, and the author therefore concludes that if the foetus is dead the entire hormone output of the placenta is taken up by the maternal circulation. These observations indicate that death of the foetus can be either primary—that is, independent of the placenta—or secondary—due to death of the placenta. Whereas in secondary death of the foetus the hormone levels in blood and urine fall rapidly, in primary death of the foetus there is no such immediate fall and the levels may even rise temporarily.

F. J. Browne.

406. **The Biological Estimation of Sex Hormones in the Pathogenic and Therapeutic Study of Habitual Abortion.** (Le dosage biologique des hormones sexuelles dans l'étude pathogénique et thérapeutique de l'avortement habituel.)

By J. THOMAS-THONNART. *Rev. méd. Liège*, **2**, 154–157, Mar. 15, 1947.

407. **The Significance of Cervical Insertion of the Placenta in the Aetiology of Abortion and of Cervico-vaginal Fistula.** (Von der Bedeutung der zervikalen Insertions der Plazenta in der Abortätiologie und die der zervico-vaginalen Fistelbildung. (Fistula cervicis uteri laqueatica.)

By O. KANNEL. *Acta obstet. gynec. scand.* **26**, 610–626, 1946. 4 figs.

Cervical implantation of the placenta praevia is uncommon. The author has found 50 such cases described in the literature, 2 of which were Finnish. Implantation may be primary or secondary; probably many of the former type lead to miscarriage and therefore are never recognized The author describes 4 patients seen in early pregnancy with vaginal bleeding, in whom the placental tissue was found in the region of the external uterine os. He has also had 2 cases, both of the secondary type, in which the condition was diagnosed as placenta praevia and Caesarean section was undertaken; only then was the cervical implantation recognized. Both these patients were of the older primigravid group, and in one much of the uterine cavity was distorted by fibroids. Hysterectomy was performed after Caesarean section on account of the uterine pathology in the one case, and because of marked bleeding from the placental site in the other. Microscopy showed the erosion of chorionic villi in the cervical area. The author suggests that this erosion from undiagnosed cervical implantation of the placenta may be a cause of the rare cervico-vaginal fistula.

Kenneth Bowes

408. **The Value of Hormonal Diagnosis in Hydatidiform Mole and Chorionepithelioma.** [In English.]
By S. GENELL. *Acta obstet. gynec. scand.*, **26**, 555–564, 1946. 52 refs.

The author has investigated the concentration of urinary gonadotrophin in 62 cases of normal pregnancy, 31 cases of hydatidiform mole, 11 cases of chorionic carcinoma, and 31 cases of hyperemesis gravidarum. His results do not accord with the original belief of Zondek that a diagnosis of hydatidiform mole and chorionic carcinoma was confirmed by the finding of high titres of gonadotrophin. The results in normal pregnancy gave figures between 1,000 and 50,000 units per litre. The figures for hydatidiform moles were often below 1,000, while over a third of the cases showed less than 10,000 units. (Half of the normal pregnancies investigated had between 10,000 and 50,000 units per litre.) With chorionic carcinoma the figure was usually less than 10,000; in fact, not greater than with a normal pregnancy. The highest figures were obtained when hyperemesis gravidarum complicated pregnancy, over one-third of the cases giving values of between 100,000 and 300,000 units per litre. The literature on this subject is extensively reviewed.

Braithwaite Rickford

409. **Report of Two Unusual Cases of Hydatid Mole.**
By L. GOHSTAND. *Med. J. Austral.*, **1**, 434(b)–435, Apr. 5, 1947. 3 refs.

410. **Case of Ovarian Cyst in Connection with Delivery.** [In English.]
By I. VIKBLADH *Acta obstet. gynec. scand.*, **27**, 11–16, 1947. 22 refs.

411. **Pregnancy Complicated by Double Uterus, Cervix, and Vagina.**
By J. KLEIN. *Amer. J. Obstet. Gynec.*, **53**, 321–323, Feb. 1947. 2 refs.

412. **Abnormal Hypertrophy of the Breasts in Pregnancy.** (Sulla abnorme ipertrofia mammaria gravidica.)
By L. CUSMANO. *Ginecologia*, **12**, 189-200, July-Aug. 1946. 2 figs., 22 refs.

Abnormal hypertrophy of the breasts in pregnancy is due to an excessive development of the breast glands—an exaggeration, as it were, of their normal changes. Sixteen cases of this rare affection have been published since 1943. To these the author adds a case of his own, and discusses the differential diagnosis and pathogenesis.

A 35-year-old multipara noticed abnormal painful swelling of her breasts from the third month of pregnancy. A similar though lesser swelling had occurred during her two former pregnancies, but had subsided soon after abandonment of breast-feeding. Clinical and laboratory findings were normal. On examination there was an enormous symmetrical enlargement of the breasts, which reached the inguinal folds. The temperature of the breasts was raised, the surface smooth and of a uniform hardness without any isolated glandular swellings. Deep palpation caused no pain; a few drops of a dense milky fluid could be squeezed out. There were no enlarged axillary lymph nodes. Two days after a normal confinement the onset of milk secretion was marked by acute breast pain, increased local temperature, and a still greater turgor of the breasts. Owing to the formation of the nipples it was possible to extract only a few drops of milk. Attempts at breast-feeding had to be abandoned, and an incipient mastitis was successfully treated with ichthyol dressings. In the absence of any other treatment regression of the swelling was immediate, until, 3 months after confinement, the size was almost normal.

In the diagnosis of abnormal hypertrophy of the breasts in pregnancy, the following points were considered: the history of the two former pregnancies, the bilaterality of the condition, the uniform and progressive enlargement of the breasts beginning in the early months of pregnancy, the absence of nodules and lymph-node enlargement, and the good general condition of the patient. There are cases in which the differential diagnosis from bilateral lymphoblastoma is difficult. The bilateral and uniform development, though characteristic of hypertrophy, cannot exclude a neoplastic factor. It is presumed that these cases of abnormal hypertrophy of the breast are due to a hypersecretion of follicular hormone. Normally the development of the breast in pregnancy is due to two hormonal factors; one which develops the ducts (folliculin), and another which develops the acino-lobular system (lutein). For the establishment of milk secretion it is necessary for these two hormones to cease to exert their influence and for a third hormone—galactin—to appear. Cases have been

observed in which the hypertrophy reappeared in 2 to 5 successive pregnancies. Spontaneous regression of the hypertrophy is so frequent that intervention is rarely indicated. The logical treatment is the giving of androgens, which inhibit the effect of folliculin and arrest the hypertrophy. Even in high dosage up to 300 mg. androgens have not been found to harm either the pregnancy or the foetus. Breast-feeding is usually impossible in these cases and, provided that it is avoided, regression of the breasts to normal is usually speedy.

Hilde Eisner

413. **Chronic Vasomotor Rhinitis in Pregnancy.**
By S. L. Fox. *Bull. Sch. Med. Maryland,* **31,** 104–107, Jan. 1947. 4 refs.

414. **Ileus in Pregnancy.** (Ileus vid graviditet.)
By E. von Post. *Nord. med.,* **33,** 744–748, Mar. 21, 1947. 55 refs.

415. **Carcinoma of the Rectum and Childbirth.** (Carcinoma del retto e stato puerperale.)
By L. Molinego. *Ginecologia, Torino,* **13,** 17–36, Jan. 1947. 13 refs.

416. **Perforated Carcinoma of the Large Intestine Complicating Pregnancy. Successful Operative Management.**
By W. B. Swartley, Z. B. Newton, J. C. Hartman, and J. W. Stayman. *Ann. Surg.,* **125,** 251–256, Feb. 1947. 3 figs.

417. **Complete Heart Block in Pregnancy. (Report of Two Successful Deliveries.)**
By T. J. Quintin. *Canad. med. Ass. J.,* **55,** 600–601, Dec. 1946. 1 fig., 6 refs.

Complete heart block is a rarity among pregnant women, 14 cases only having been recorded up to 1938. The author describes a patient who had two normal pregnancies and confinements. Symptoms were negligible except for slight dyspnoea on exertion during the last 2 months before the second confinement and some giddiness after stooping. Laboratory investigations did not reveal the cause of the heart block.

Braithwaite Rickford

418. **Acute Leucemia and Pregnancy. Report of Fatal Case Treated with Penicillin.**
By R. Harris, I. G. Tchertkoff, and L. Greenwald. *Amer. J. Obstet. Gynec.,* **53,** 142–149, Jan. 1947. 3 figs., 16 refs.

419. **Pregnancy and Sickle-cell Anemia.**
By R. E. Martinak. *Amer. J. Obstet. Gynec.,* **53,** 332–334, Feb. 1947. 7 refs.

420. **Diabetes Mellitus in Pregnancy.** (Om forlobet af diabetes mellitus i graviditeten. Et tilfælde af coma diabeticum med excessiv acidose efterfulgt af normoglykæmi og aglykosuri efter fodselen.)
By V. P. Petersen. *Nord. med.,* **33,** 539–541, Feb. 28, 1947. 13 refs.

A 32-year-old woman had a history of two stillbirths, one due to development of a contraction ring, the other to foetal asphyxia. Her third pregnancy was normal until the seventh month, when she suddenly developed thirst and polyuria and went into coma a week later. She had a profound acidosis, plasma bicarbonate being reduced to 2.4 millimols per litre; there were sugar, protein, and acetone in the urine, and the blood sugar was 330 mg. per cent. Treatment with isotonic sodium bicarbonate solution, insulin, and glucose relieved her coma, and she gave birth to a macerated foetus. Immediate improvement in her diabetes ensued, the blood sugar returning to normal and the sugar disappearing from the urine. However, 18 months later, diabetes developed. Similar cases of transient diabetes occurring in pregnancy are referred to, the author pointing out the tendency for the condition to be associated with acidosis and coma in late pregnancy. The possibility that foetal death was the factor precipitating coma in this case is discussed.

S. S. B. Gilder

421. **Pelvic Osteo-articular Tuberculosis and Pregnancy.** (Tuberculosi osteo-articolare del bacino e gravidanza.)
By T. Teresio. *Ginecologia,* **12,** 201–217, July-Aug. 1946. 2 figs., 27 refs.

Pelvic osteo-articular tuberculosis is rare, and its occurrence as a complication of pregnancy is exceptional. A secondary tuberculous osteitis is followed by invasion of a pelvic joint. Predisposing causes, according to some authors, are the increased genital activity during pregnancy (and puberty), the lessened resistance to infection at this time, the disturbed endocrine balance, the tendency to decalcification, and a number of traumatic factors, including those accompanying birth.

Considering the extreme rarity of the disease, the nearly simultaneous observation of 2 cases by

the author is of interest. The cases reported so far in the literature mostly concern multiparae, already known to have tuberculosis of bones or lungs, and in whom pregnancy was responsible only for a secondary localization of the disease in the pelvis. In contrast, the 2 cases observed by the author occurred in primiparae with no history of tuberculosis. As a rule the disease has no harmful influence on the course of the pregnancy. Only in exceptional cases, usually complicated by tuberculosis of the spine, is interruption of the pregnancy necessary, owing to the reduced volume of the abdominal cavity with circulatory and respiratory disturbances.

The influence of pregnancy on the course of the pelvic osteo-articular tuberculosis is disastrous, particularly when the first manifestations of the disease appear in the early months of pregnancy. In Case 1 the tuberculous lesion, localized in the left sacro-iliac joint, was already evident in the third month, while the tuberculous lesion of the os pubis in Case 2 caused symptoms in the last weeks of pregnancy. In the first case the condition of the patient became progressively worse in the second half of the pregnancy, and more so in and after the puerperium; the second case was then clinically healed. Neither before nor after confinement was it possible to detect a primary active focus from which the tubercle bacilli may have entered the blood stream to settle in the pelvis. Possibilities are the spread from a lymph node or the " flare-up " of a clinically silent tuberculosis of the pelvic bone. Among the causes predisposing to osteo-articular pelvic tuberculosis during pregnancy the diminution of the calcium content of the blood serum deserves particular attention. The localization in the pelvis may also be favoured by a decalcification of its bones.

Treatment in both cases consisted of a generous diet with the giving of calcium and vitamins and the use of ultraviolet irradiation. The author discusses the question of interruption of pregnancy in these cases. Where the patient's condition is deteriorating or the tuberculous process appears to be spreading, interruption is indicated if pregnancy is in a relatively early stage. The most satisfactory method of interruption is by the use of X-rays. Operative interference is deprecated on account of the possibility of disseminating the tuberculosis. The condition occasionally has an unfavourable influence on the confinement, but more often the effect of the lesion on the pelvic joints leads to easier confinement. With regard to the effect of the confinement on the tuberculosis, cases are seen in which a flare-up of the disease has occurred early in the puerperium, and occasionally a miliary tuberculosis has followed. Rupture of the pelvis with a fatal outcome has also been known to occur.

Hilde Eisner

422. **Development of Pulmonary Tuberculosis after childbirth.** (Evolución de la tuberculosis pulmonar después del parto.)

By V. M. Aviles, F. Rodriguez, J. Oneto, and H. Ampuero. *Bol. Soc. chil. Obstet. Ginec.*, **11**, 145–166, Oct., 1946. 9 figs., 15 refs.

423. **Pregnancy and Renal Tuberculosis.** (Gestacion y tuberculosis renal.)

By L. Tisne Brousse. *Bol. chil. Obstet. Ginec.*, **11**, 204–211, Oct. 1946.

424. **On Miliary Tuberculosis in Association with Pregnancy and Delivery or Abortion.** [In English.]

By P. Lundström. *Acta obstet. gynec. scand.*, **27**, 84–93, 1947. 29 refs.

425. **Pregnancy and Typhoid—Paratyphoid Fever.** [In English.]

By H. Sauramo. *Acta obstet. gynec. scand.*, **27**, 58–69, 1947. 14 refs.

426. **Ectopic Pregnancy as a Diagnostic Problem. (A Study of 100 Cases.)**

By H. B. Atlee. *Canad. med. Ass. J.*, **56**, 268–273, Mar. 1947.

427. **Combined Extrauterine and Intrauterine Pregnancy.**

By L. Gruenewald. *Amer. J. Obstet. Gynec.*, **53**, 341–342, Feb. 1947. 1 ref.

428. **Ectopic Decidual Reaction.** (Reacción decidual ectópica.)

By A. Marano. *Arch. Soc. argent. Anat. norm. patol.*, **8**, 213–217, 1946. 4 figs., 13 refs.

429. **Early Form of Secondary Abdominal Pregnancy.**

By A. J. Kobak and M. A. LaIuppa. *Amer. J. Obstet. Gynec.*, **53**, 329–330, Feb. 1947. 1 fig.

430. **Abdominal Pregnancy.**

By H. F. Burkons. *Ohio. St. med. J.*, **43**, 161–164, Feb. 1947. 17 refs.

431. **An Analysis of 212 Consecutive Cases of Ectopic Pregnancy.**
By B. LEFF and S. G. WINSON. *Amer. J. Obstet. Gynec.*, **53**, 296–299, Feb. 1947. 6 refs.

432. **Maternal Pulmonary Embolism by Contents of the Amniotic Fluid.**
By C. T. HEMMINGS. *Amer. J. Obstet. Gynec.*, **53**, 303–306, Feb. 1947. 7 refs.

433. **Observations on Rupture of the Uterus.**
By H. H. CAFFEE. *Sth. med. J.*, **40**, 189–191, Feb. 1947.

See also Nos. 376, 455.

LABOUR

434. **Is Artificial Rupture of the Membranes to Induce Labour Useful?** (Ist die künstliche Blasensprengung als geburtsförderndes Mittel brauchbar?)
By H. SCHERER. *Gynaecologia, Basel*, **122**, 233–243, Oct. 1946.

When artificial rupture of the membranes is carried out in cases of contracted pelvis several days may elapse before the onset of labour. This time interval may be shortened when the uterus is sensitized before the membranes are ruptured. The author believes: (1) that the bag of membranes plays no part in the dilatation of the cervix; (2) that increased intrauterine pressure stretches the uterine wall, causing spasm of the muscle fibres so that the dilatation of the cervix by retraction of the lower uterine segment either ceases or is enormously lengthened, and labour does not progress; and (3) that decrease in intrauterine pressure in suitable cases is followed by rapid delivery.

The conditions which must be present if artificial rupture of the membranes is to be successful are: (*a*) no obvious disproportion between the foetus and the mother's pelvis; (*b*) the presenting part in the inlet; (*c*) no vaginal infection; (*d*) the cervix taken up and at least one finger dilated; and (*e*) the uterus irritable. These conditions are often difficult to obtain, and experience is necessary before it is possible to say whether rupture of the membranes will be useful in particular cases.

The three conditions in which this method is especially useful are: (1) post-maturity, especially in multiparae; (2) over-distension of the uterus with hydramnios, twins, or a large infant; and (3) uterine inertia associated with hypertonic uterus and feeble uterine contractions. In 77 out of 79 patients in group (1) artificial rupture of membranes resulted in labour within 6 hours. In the 2 remaining patients, the estimated date of delivery had been miscalculated and they were delivered, after 30 hours in 1 case and 6 days in the other, of premature infants. In group (2) there were 30 successful cases, labour starting within 6 hours. In group (3) there were 33 successful cases with delivery mainly within 2 hours after rupture of the membranes. The author states in conclusion that while he believes that with careful assessment of all the facts artificial rupture of the membranes is the most certain method of treatment in these groups, he does not rely on one method alone in the management of his cases.

Gladys Dodds

435. **The Intrauterine Use of Sulfanilamide.**
By A. SADOVSKY, Y. M. BROMBERG, and Z. POLISHUK. *Exper. Med. Surg.*, **4**, 310–318, Nov. 1946. 4 figs., 8 refs.

Investigations on the absorbability of sulphanilamide from the uterus were made on cases of Caesarean section, of incomplete abortion, and of curettage of various lesions. The degree of absorption proved to be greatest after Caesarean section and least after curettage and compared very favourable with the degree of absorption from surgical wounds. Local bacteriostasis was also examined by comparison of cultures in cases of local uterine sepsis. Out of 10 specimens growing *Staphylococcus aureus* and *albus* initially, 7 were sterile 24 hours later. Clinical application of this fact was made in a further series of suitable cases, and the authors conclude that the results showed the prophylactic as well as the curative value of sulphanilamide.

R. K. Bowes

436. **Dichorial Unilateral Tubal Twins.**
By R. S. HAUKOHL, and W. A. D. ANDERSON. *Amer. J. Obstet. Gynec*, **53**, 338–339, Feb. 1947. 1 fig., 12 refs.

437. **Monovular Twins.**
By G. H. PICKERING. *Brit. med. J.*, **2**, 988, Dec. 28, 1946.

The author records a case of twin labour which in his opinion refutes the theory of X and Y

chromosomes. The first twin, a girl, was born spontaneously and weighed 5 pounds 2 ounces (2.31 kg.) at birth; the second twin, a boy weighing 6 pounds 12 ounces (3.06 kg.), was delivered by forceps on account of deep transverse arrest of the head. Examination of the afterbirth, which came away normally after the birth of the second twin, disclosed a single bag of membranes containing 2 placentae. Detailed examination showed that there was no communication between the placentae, nor was there any evidence that there had been any fusion of the 2 gestation sacs.

T. N. MacGregor

ANAESTHETICS, ANALGESICS.

438. **Effects of Demerol in Obstetrics.**
By W. M. Mallia. *N. Y. St. J. Med.*, **46**, 2753–2756, Dec. 15, 1946. 11 refs.

Over a period of 2½ years 220 patients were given "demerol" (pethidine) with various other drugs for the production of amnesia in labour. The results were excellent in 65 per cent of cases. The drug most favoured in combination with demerol was scopolamine. Barbiturates had a depressant action on the maternal respiratory system, though no actual fatality occurred. Intramuscular injection of demerol, 2 ml. 2-hourly, and of 1/200 gr. (0.32 mg.) scopolamine 3-hourly was the routine administration. In short, rapidly progressing labours intravenous injections were given of 2 ml. demerol and 5 minutes later of 1/100 gr. (0.65 mg).) scopolamine, and 1 hour later an intramuscular injection of scopolamine. Premedication for Caesarean section by demerol and scopolamine was also tried; the effect was good if local analgesia followed (with general anaesthesia after this premedication there were disastrous foetal results). In a subsequent discussion of this paper it was pointed out that with such a technique all patients need careful nursing and watching as there was reduced mental alertness.

R. K. Bowes

439. **The Critical Analysis of 250 Deliveries Under Continuous Caudal Analgesia.**
By J. H. Prince. *Ohio St. med. J.*, **43**, 274–275, Mar. 1947.

440. **A Statistical Study of Delivery with Continuous Caudal Analgesia, as Compared with Other Methods.**
By S. D. Collins, F. R. Phillips, and D. S. Oliver. *Publ. Hlth. Rep., Wash.*, **51**, 1713–1735, Nov. 29, 1946. 14 figs., 28 refs.

The authors are statisticians in the United States Public Health Service. With the collaboration of clinical colleagues they have assembled data referring to the use of continuous caudal analgesia in 2,516 mothers delivered in the Philadelphia Lying-in Unit of the Pennsylvania Hospital, between May 1943, and August 1945. Of these patients 82.2 per cent obtained complete relief without any supplementary analgesic, a further 8.2 per cent had complete relief with supplementary analgesics, 4.3 per cent received partial relief, and 5.3 per cent experienced no relief. The average duration of caudal analgesia in the series is recorded as 3 hours, with a statistical median of 2.2 hours. One-third of the mothers showed a marked drop in systolic blood-pressure after analgesia was started. The average blood loss was 127 ml. and 8.6 per cent of the patients lost more than 250 ml.

An attempt is then made to compare the results with a control series of 1,024 mothers delivered in the same hospital between December 1942, and July 1943. After analysis of the incidence of complications in the two series the authors conclude that a comparison is justifiable. They demonstrate operation rates of 84.5 per cent in the caudal analgesia group and of 69 per cent in the control series. This is mainly accounted for by an increase in the use of outlet forceps from 56.4 to 68.3 per cent. The third stage of labour was shorter in the caudal analgesia series by a statistically significant figure, and the incidence of febrile maternal morbidity was also significantly lower. Stillbirths and neonatal deaths were less frequent in the patients receiving caudal analgesia, the total loss being 20.6 per 1,000 live births in the caudal analgesia series as against 45.6 per 1,000 live births in the control series—a difference of statistical significance. Maternal deaths in each series (2 in each) were too few to permit of profitable comparison. The authors conclude that there was no evidence of danger to the mothers delivered under caudal analgesia despite the increased incidence of operative delivery, and that the outlook for the foetus is

favourably influenced by the use of this method.

[Although the mathematics of this analysis are sound, the conclusion that the better results are due to the use of the method cannot be accepted. The control series is not synchronous with the other. While the authors claim that the patients receiving caudal analgesia represent " an unselected group except for the inclusion of a few with heart disease ", no reference is made to the numbers of patients in the Philadelphia Lying-in Hospital not submitted to caudal analgesia at the time of the study, and it seems probable that some form of selection must have existed. The " controls " are loaded unfavourably in respect of foetal mortality, reference to the authors' tables indicating a proportion of babies weighing less than 4 pounds 8 ounces (2 kg.) considerably higher in the control series than in the cases under investigation, although the incidence of babies weighing 5 pounds 8 ounces (2.46 kg.) and less is similar in both series. Furthermore, while the incidence of complications arising during pregnancy and during delivery is approximately the same in both series, the detail of the complications is not analyzed in this paper. The numbers are comparatively small in both series, and important loading of one or other with an unusual incidence of such complications as placenta praevia, accidental haemorrhage, or foetal monstrosity might well have occurred. It is also permissible to speculate whether the extremely careful attention which the caudal analgesic patients were given during the investigation might not have been expected *per se* to contribute to slightly improved results. Nevertheless, the article is a reassuring contribution to our knowledge, in that it records very good results in respect of foetal and maternal mortality and morbidity obtained by a method which gives a high incidence of relief of pain at the expense of an increased incidence of operative delivery. Most British practitioners would consider the rate of operative delivery much too high even in the control series.]

W. I. C. Morris

441. **Amnesia During Parturition. Use of Pentobarbital Sodium and Scopolamine Hydrobromide.** By P. P. VOLPITTO. *J. Amer. med. Ass.*, **132**, 1059–1062, Dec. 28, 1946. 1 fig., 17 refs.

The author reports on the use of pentobarbitone sodium (" nembutal ") and scopolamine hydrobromide intravenously in 170 obstetric cases. The object was to obtain amnesia, not analgesia or anaesthesia. The contents of a pentobarbitone sodium ampoule (0.25 g.; 3¾ gr.) and a scopolamine hydrobromide ampoule (0.00064 g.; 1/100th gr.) are mixed and diluted to 10 ml. with sterile distilled water. Each ml. of this dilution thus contains 0.25 g. of pentobarbital sodium and 0.000064 g. of scopolamine hydrobromide. In normal primiparae or multiparae, as soon as regular pains develop—4 to 5 minutes apart and lasting 30 or more seconds—the combination is given intravenously. An initial 3 or 4 ml. of the mixed agents is given fairly rapidly at the rate of 1 ml. every 5 or 10 seconds; then the injection is slowed to the rate of about 1 ml. every 30 seconds, until the patient either begins to fall asleep or talks incoherently. At this point the injection is stopped, but the needle is kept in place and the patient is watched during a uterine contraction. If she is extremely restless during this pain and talks coherently an additional 1 to 3 ml. at the most is administered. On the other hand, if the patient is slightly restless or opens her eyes and talks incoherently no further injection is given. The average patient, whether primipara or multipara, will require a total initial injection of 10 ml. of the mixture. As little as 6 ml. and as much as 20 ml. has been found necessary in some cases. A patient whose cervix is fully dilated and who is beginning to bear down with each pain may require greater initial or additional amounts. However, extreme caution is necessary at this time as amnesia and not analgesia is sought; hence more restlessness should be expected at this time. Care must be taken not to mistake momentary lucid intervals, such as recognition by the patient or the request for the relief of pain, as indications for administration of more drugs. After the initial induction of amnesia the frequency and amounts of further injections will depend on the particular patient and the progress of labour. When the patient tends to become restless during the pain or does not sleep and is somewhat lucid between uterine contractions, the administration of more of the drugs is indicated. This will generally occur about three quarters to 1 hour after the first injection, and not more than 2 ml. of the diluted mixture will be required. The average multipara, unless the cervix is fully dilated

at the start, will need yet another 2 ml., and the average primipara about three such injections. The interval grows longer with each injection—that is, 1 hour for the first, 2 hours for the second, and 3 to 4 hours for the third.

In the 170 women there were 75 primiparae and 95 multiparae; 96.4 per cent delivered spontaneously and 3.5 per cent required low forceps. Complete amnesia was reported by 89.4 per cent, and partial amnesia by 10.6 per cent. In 16.6 per cent there was an apparent slowing of either the first or the second stage and in 2.9 per cent, labour pains ceased completely after the administration of the drugs. Three patients (1.7 per cent) became extremely excited and almost unmanageable in the early second stage; 20 per cent became "exceedingly restless" during the latter part of the second stage. A severe drop in blood-pressure occurred in 2 patients and was associated in both with a too rapid injection; both quickly recovered on intravenous injection of 2 mg. of "neosynephrine" hydrochloride and administration of a high concentration of oxygen. Too rapid injection caused severe respiratory depression in 1 patient. Nausea and vomiting occurred in 3 patients. There was one maternal death; this patient had been given 15 ml. of the mixture in two injections and shortly after the second became cyanotic and dyspnoeic with a pulse rate of 160 and systolic and diastolic blood-pressure of 70 and 40 respectively; 2 hours later a stillborn foetus was delivered by high forceps. Of the infants, 92.4 breathed spontaneously immediately after birth and 7.6 were apnoeic, all but 1 being successfully resuscitated. The author concludes that the method is an efficient and safe one for obtaining satisfactory amnesia during labour.

F. J. Browne

442. The Use of Rectal Pentothal Sodium in Obstetrics.

By E. W. Fergurson. *North Carolina med. J.*, **8**, 84–86, Feb. 1947. 9 refs.

Thirty obstetric cases are reviewed in which rectal pentothal, in conjunction with "demerol" (pethidine) and scopolamine intramuscularly, was employed for analgesia. While it is appreciated that no absolute conclusions can be drawn from this small series of cases, the paper is presented in the hope that it will stimulate further study on the use of rectal pentothal in obstetrics. The author has observed that the intramuscular administration of demerol in doses of 50 to 100 mg. and of scopolamine in doses of 1/200 gr. (0.32 mg.) during the first stage of labour greatly enhances the action of rectal pentothal. By combining the drugs he has found that a single dose of 1 g. per 65 pounds (30 kg.) of body weight is sufficient to maintain analgesia in practically every case, whereas the dose of pentothal previously recommended for prolonged analgesia was 1 g. per 50 pounds (23 kg.) body weight, followed about 1½ hours afterwards by a further 1 g.

The pentothal is administered by rubber catheter into the rectum when the cervix is dilated to about 3 cm. in multiparous patients and to 4 cm. in primiparae. The dose required is calculated on the patient's weight as recorded at the last prenatal visit. A sensation of drowsiness and tingling in the extremities usually follows within 2 to 5 minutes. Occasionally during the second stage of labour it may be necessary to give inhalations of nitrous oxide and oxygen to avoid administration of further pentothal. With the technique described complete analgesia and amnesia was obtained in all except 2 of the mothers in the series. These 2 were the first patients delivered in the clinic by this method, and neither demerol nor scopolamine had been employed. In practically every case the patient slept continuously. Drowsiness and relaxation frequently continued for from 2 to 8 hours. The author believes that the first stage of labour is shortened by the use of rectal pentothal and that there is no increased tendency to haemorrhage, relaxation of the uterus, or placental retention.

No maternal or foetal death was recorded. Three babies required cardiac or respiratory stimulation, but the author considers that in none of them was the difficulty attributable to the drug. Throughout the series no untoward maternal reactions to the drug were noted. Pentothal is contra-indicated in patients with respiratory or cardiac embarrassment. The drug may have a depressant effect on the respiratory centre of the foetus, and particular care must be exercised in cases of prematurity; similar caution is required in pre-eclampsia. "Nembutal", "seconal", and other barbiturates should not be used in conjunction with rectal pentothal.

R. L. Hartley.

443. **Sodium Pentothal Anesthesia in Major Obstetric and Gynecologic Surgery. Preliminary Report of 300 cases.**

By V. P. MAZZOLA. *Amer. J. Obstet. Gynec.*, **53**, 207–213, Feb. 1947. 2 refs.

PUERPERIUM

444. **The Effect of the Anticoagulants on Postpartum Bleeding.**

By A. C. BARNES and H. K. ERVIN. *Surg. Gynec. Obstet.*, **83**, 528–530, Oct. 1946. 1 fig., 7 refs.

The anticoagulants dicoumarol and heparin might be useful in the treatment of puerperal thrombophlebitis. But is their use likely to increase vaginal bleeding or to cause postpartum haemorrhage? To get more accurate information on this point the authors measured vaginal blood loss in patients receiving these two drugs in the early puerperium. Blood-loss studies beginning 1 hour postpartum and continuing during the patients' stay in hospital were made on 30 consecutive primiparous women who had had normal labours at term. All perineal pads were collected over the period the patient was in hospital; the pads of the preceding 24 hours were washed out daily in a measured volume of water and the haemoglobin measured in the wash water. Prothrombin levels and clotting times were determined for all these patients, 14 of whom were given dicoumarol and 5 heparin; 11 control patients received neither.

The dicoumarol was given in doses adequate to depress prothrombin levels to the therapeutic range—300 mg. during labour, 200 mg. on each of the first 2 days postpartum—while subsequent doses were adjusted by the prothrombin determinations. The drug was discontinued 24 to 48 hours before the patients left hospital. Graphs show the average daily prothrombin level and the average blood loss for patients receiving dicoumarol and for control patients. There was no significant difference in the average blood loss in the two series. Bleeding and clotting time in the nursing babies showed prolongation in one-third of the cases.

The action of heparin is more rapid, and the drug was used more cautiously to obtain a prolonged clotting time only for a 24-hour period on either the first or second day postpartum; considerable increase in the clotting time was observed, but no increased vaginal bleeding. Patients with thrombophlebitis were not treated, the study being undertaken to determine whether or not, should these drugs be indicated, increased vaginal bleeding prohibited their use. The series is small, but the data obtained showed that these two drugs are not necessarily contra-indicated in the puerperium.

Eardley Holland

445. **Puerperal Inversion of the Uterus.**

By R. TORPIN. *J. med. Ass. Georgia*, **36**, 63-69, Feb. 1947. 6 refs.

446. **Complete Absence of Lochia Following Delivery. Report of a Case.**

By R. J. HEFFERNAN and C. L. SULLIVAN. *New Engl. J. Med.*, **236**, 65–67, Jan. 9, 1947. 12 refs.

On account of toxaemia of pregnancy, breech presentation, and disproportion, an elderly primigravida was delivered by lower segment Caesarean section after pregnancy had lasted 36 weeks. No lochia at all was passed and on the twenty-first day after delivery the patient menstruated normally. Periods continued at 28-day intervals afterwards. The puerperium was apyrexial.

[It appears probable that in this case membranes obstructed the internal os. There is no mention of any step being taken, in the course of the operation, to find out whether the cervix was left patent.]

D. M. Stern

447. **An Outbreak of Puerperal Infection in a Maternity Home Caused by Sulphonamide-Resistant Streptococci.**

By A. A. MILLER and P. KIDD. *Mon. Bull. Min. Hlth.*, **5**, 245–248, Nov. 1946. 1 ref.

The authors, working at the Emergency Public Health Laboratory, Reading, England, record an outbreak of puerperal fever in a small maternity hospital in which 8 out of 11 patients were involved. There had been puerperal pyrexia in some earlier cases in which it had not been customary to collect bacteriological specimens, but simply to administer sulphathiazole. In the outbreak recorded in the present paper, sulphathiazole was not as effective as previously, and so bacteriological investigations were carried out. Haemolytic streptococci were isolated from 8 vaginal swabs, and all belonged to Group A and Type 19. Further, when the sensitivity of the strains to sulphonamides was tested

all were found to be resistant to 1 mg. per 100 ml., and 6 out of the 8 to 5 mg. per 100 ml. of sulphanilamide and sulphathiazole. Some of the cases required penicillin to effect a cure. The home was closed for 2 weeks and thorough sterilization and disinfection were carried out, but when patients were readmitted there was a further infection. Throat and nose swabs from the staff were examined; one only showed haemolytic streptococci, but this did not belong to the same type as the strains isolated from the patients. The presumption was, therefore, that case-to-case infection had taken place. The lesson to be learnt from this outbreak is that, despite the undoubted value of sulphonamides, bacteriological examination is still necessary in cases of puerperal pyrexia, and the same measures of control should be adopted as in the pre-sulphonamide days.

J. Smith

448. **A Case of Puerperal Septicaemia due to Fusiformis Necrophorus.**

By T. V. Cooper and J. A. Robson. *Mon. Bull. Min. Hlth.*, **6**, 10–12, Jan. 1947. 1 fig., 4 refs.

After a brief survey of the literature the authors describe a case of puerperal septicaemia due to the *Fusiformis* group of organisms. The description includes a case report with full temperature chart and a detailed account of laboratory investigations. Colonies of the organism appeared on the surface of sedimented blood after 72 hours' anaerobic incubation at 37°C. The organism was sensitive to penicillin *in vitro*. The patient responded quickly to penicillin treatment. Convalescence was uneventful and the patient was normal 5 months later.

R. H. Parry

449. **The Treatment of Acute Postpartum Thrombophlebitis of the Lower Extremity by Continuous Caudal Anesthesia.**

R. C. Benson. *Amer. J. Obstet. Gynec.*, **52**, 830–836, Nov., 1946. 14 refs.

Five cases of acute postpartum thrombophlebitis of the lower extremity (3 deep femoral and 2 superficial saphenous) were treated by continuous caudal analgesia. The method is based on the theory of Leriche and Kunlin (1934) that vasospasm is the important factor in the thrombophlebitic process and the practical application of this theory in the treatment of the condition by sympathetic nerve block following paravertebral injections of local analgesics, a method popularized particularly by Oschner. The success of continuous caudal analgesia in relieving pain and spasm in obstetrics suggested that the same method might be effective in overcoming the pain and vasospasm in acute thrombophlebitis.

Thirty ml. of 1.5 per cent "metycaine" in Ringer's solution was injected into the sacral space through the sacral hiatus. Twenty ml. of the solution was injected (hourly for 4 hours or more) through the sacral needle which remained in position throughout the period of treatment, during which the patient lay on the side or back with the legs a little elevated. Pain was relieved in about 15 minutes, and was not likely to return during the course of 12 or more hours of treatment. Temperature returned to normal in 12 to 24 hours, oedema subsided in about 24 hours, and tenderness disappeared in about the same time. "Pontocaine" 0.15 per cent with 30 ml. as an initial dose, was used in some of the cases. The method is stated to be particularly applicable to acute cases; it is doubtful if it is likely to be beneficial in chronic cases.

T. C. Clare

450. **Acute Postpartum Necrosis of the Anterior Hypophysis.**

By E. W. Nelson and J. P. Michaels. *Amer. J. Obstet. Gynec.*, **52**, 817–825, Nov. 1946. 2 figs., 16 refs.

A woman, aged 32, primigravida, was admitted in labour at 8½ months with generalized tonic and clonic convulsions; her blood-pressure was 207/160 mm. Hg. The onset of labour was spontaneous and delivery assisted by low forceps. Blood loss was moderate (400 ml.). The patient passed into a condition of shock immediately after the expulsion of the placenta and blood-pressure fell to 78/50 mm. Hg. Blood transfusion had no effect on the blood-pressure, which, however, rose to 90 to 100 mm. systolic after intravenous injections of adrenaline. Urinary output was very scanty during the next 24 hours, but there was slow improvement after large doses of intravenous hypertonic glucose. Because of anaemia she was given 500 ml. of citrated blood, followed in error by the infusion of a litre of distilled water. Twelve hours later the patient was

apparently moribund; however, there was dramatic improvement after the intravenous administration of 300 ml. of 5 per cent sodium bicarbonate followed by 50 ml. of 50 per cent glucose. This was given because of a clinical impression of hypoglycaemia. More glucose was administered to combat a relapse into a semi-comatose condition. It was noted that all this glucose failed to raise the blood-sugar level or to promote glycosuria.

The continued necessity for the use of 50 per cent glucose on account of coma led to the decision that this case was one of anterior pituitary necrosis. "Antuitrin" therapy was begun but no improvement was noted after 12 hours. The next day treatment was started with desoxycorticosterone acetate (DOCA) in conjunction with sodium chloride administration, 20 mg. of DOCA being given in the first 24 hours with a maintenance dose of 15 mg. daily afterwards. Some improvement followed; but an attempt to reduce the dose of DOCA was followed by a relapse into coma, with mild convulsions. On the 15th day the patient was allowed to get up in a chair, but two days later thrombophlebitis developed in the right saphenous vein. The saphenous and femoral veins on that side were ligated and lumbar sympathetic block was performed. A general septic condition gradually supervened and the patient died a month after the delivery. At necropsy, the pituitary weighed 0.506 g. In the anterior lobe 85 per cent of the gland substance was occupied by a yellow depressed area and the entire anterior lobe stained pink without any cellular details. The posterior lobe was normal.

[A point of particular interest about this case is that the diagnosis of anterior lobe necrosis was made within a few days of delivery, not from symptoms described by Simmonds as characteristic, for these symptoms did not develop till a later period, but from "a clinical impression" of hypoglycaemia. There is at present no specific treatment of the condition in the acute stage, though the line of treatment followed here—namely, by hypertonic glucose and DOCA (to stimulate glucogenesis)—might have proved successful if it had not been for the thrombophlebitis, presumably started by the very concentrated glucose injections). *T. C. Clare*

451. **Treatment of Breast Abscesses with Penicillin.** By M. E. FLOREY, J. S. MACVINE, and M. A. M. BIGBY. *Brit. med J.*, 2, 845–848, Dec. 7, 1946. 2 figs., 18 refs.

The authors have taken considerable trouble and time over this investigation of 34 cases.

TABLE I.

Comparison of Results in Breast Abscesses

	No. of Cases	Duration in Days after First Treatment of					
		Pyrexia		Suppuration		Healing Time	
		Mean ±S.E.	S.D.	Mean ±S.E.	S.D.	Mean ±S.E.	S.D.
Controls	16	7.5±1.97	±7.86	13.8±3.0	±12.0	26.5±2.45	±10.17
Treated	18	3.9±0.91	±3.73	6.3±0.82	± 3.5	13.5±1.50	6.37
Difference		3.6±2.17		7.5±3.11		13.0±2.87	

S.E. = Standard error of mean. S.D. = Standard deviation.

The 16 controls were treated by one or two courses of 20 to 30 g. of either sulphathiazole or sulphamezathine; the abscesses were drained surgically, and the wounds were dressed or irrigated with eusol and subsequently treated with acriflavine and lotio rubra. A course of 30 to 65 mg. of stilboestrol was given over a period of three to five days. In 18 cases treated with penicillin, stilboestrol was given to only three patients. The decision to administer penicillin depended upon the state of the breast when first seen. In 13 cases *systemic penicillin* was given by the intramuscular route in a dosage of 15,000 units 3-hourly for a duration of 12 hours as a minimum and 3½ days as a maximum.

Aspiration and injection of penicillin under local analgesia once in 24 hours was performed in 10 abscesses as soon as fluctuation could be detected. A West Middlesex needle and stylet were used, and the puncture was performed through intact firm skin. All pus was evacuated and 120,000 units of penicillin in saline, equivalent to two-thirds of the volume of pus removed, were injected into the cavity if the inflammation was not fully localized; if it was localized 500 units per ml. were injected into the cavity, the puncture being sealed with collodion. If there was more than one abscess each was given similar treatment. The abscesses so treated contained not more than 10 ml. of pus and required daily aspiration and injection for 4

to 7 days. *Instillation of penicillin after expression of pus* was performed on 5 abscesses. Spontaneous discharge of pus under systemic administration of penicillin was treated by the expression of pus every 24 hours and instillation along the sinus of penicillin through a suitable catheter or needle, the sinus being closed by collodion. A combination of the two methods of local treatment was employed in 5 abscesses, a needle being left in the abscess cavity and instillation performed through it. Sinuses developed along this tract in a day or two, and this added a week to the healing time, but the authors noted that the patient's comfort was very much greater. *Instillation following incision and suture* was performed on 4 abscesses. These were abscess cavities containing 100 ml. or more. The abscesses were drained through intact firm skin and a rubber tube was snugly sutured in position. Pus was expressed through this tube and instillation performed through it twice a day for 4 to 8 days. The authors again noted that this was a very comfortable method for the patient, and patients preferred instillation to intramuscular injection or aspiration and injection. They state that little work on penicillin in breast abscesses has been reported, and reiterate that the social problems of this malady are considerable. They consider that now that penicillin is freely available large systemic doses and surgical incision might eliminate sepsis as rapidly as the employment of small doses of penicillin systematically and local instillation. They emphasize that if local instillation is used a rigid technique and experience are necessary.

TABLE II.

	Control	Treated
Total number of days spent in hospital	348	191
Total period of out-patient treatment	313	41
Total	661	232

In the penicillin series the healing time was half that of the controls, and suppuration was hastened rather than retarded [with the dose of penicillin employed] but subsided more rapidly. Stilboestrol was unnecessary and the mother continued suckling throughout treatment. The number of operations [general anaesthetics] was reduced from 22 to 4. [The number of surgical procedures with or without local analgesia appeared to be many, however.] The total number of days of treatment was reduced from 661 to 232.

[In respect of healing time the authors have shown again that penicillin is the chemotherapeutic agent of choice in the treatment of breast abscesses. Is it not time that sulphonamides should be abandoned in this type of case Unfortunately in the past a recurrence of the disease some time later has not been uncommon. A follow-up of 1 to 6 weeks is not an absolute indication that these cases will not recur. This penicillin investigation has been very valuable, but the authors' technique and dosage will not necessarily be accepted as the method of choice. Systemic penicillin is essential to abort the early case or to localize the abscess; Taylor and Way (*Brit. med. J.*, 1946, **2**, 731) have recently emphasized this point. Other workers have found that a dose of 60,000 units 3-hourly is infinitely superior to one of 15,000. Many patients are intolerant of, and find extremely painful, aspiration and injection under local analgesia, The authors themselves comment on the fact that patients whose abscesses had undergone spontaneous rupture or were afforded reasonable drainage were much more comfortable. Breast abscesses are a social calamity, and it is probable that lack of space in periodicals has prevented other workers from publishing their results. In March 1946, in a progress report to the Medical Research Council, the Middlesex Hospital staff stated that after a trial of various methods a dose of 60,000 units 3-hourly and temporary drainage of an abscess—if it formed—by means of a ¼-inch (0.6 cm.) incision gave the best results. A follow-up of one year showed no recurrence.]

R. Vaughan Hudson

THE INFANT.

452. **Intracranial Damage in the Newly Born.** By T. Y. NELSON. *Med. J. Austral.*, **1**, 268–270, Mar. 1, 1947. 7 refs.

The author deals with the clinical diagnosis of established cases of intracranial haemorrhage, with special reference to active treatment. The particular group considered is that in which the damage

is apparently great and the symptoms so severe that survival of the infant is in doubt. Haemorrhage into the subdural space constitutes the largest group, as well as the most important one as regards the probability of successful treatment, whether to save life or to prevent disabling sequelae. Tentative diagnosis may be confirmed by needling through the coronal suture lateral to the fontanelle. Improvement often follows the withdrawal of even a small amount of blood. Gradual decompression by the withdrawal of small quantities daily is recommended. In some cases, after 2 or 3 weeks, a burr hole may be made in the temporal region for the withdrawal of more blood or for exploration.

Over a period the author has examined a number of infants with a tentative diagnosis of this lesion, and the presence of haemorrhage has been established in 6. Of these 4 developed normally after active treatment and 2 were left with spasticity and mental defects. The series is a small one but, as the author states, it is presented in the hope that further interest may be stimulated in an important and difficult subject.

Eardley Holland

453. **Bilateral Harelip and Unilateral Harelip with Cleft Palate in Fraternal Twins.**

By P. A. SHEA and R. B. NELSON. *Amer. J. Obstet. Gynec.*, **53**, 340, Feb. 1947. 1 ref.

454. **Sympus Apus. A Case Report.**

By L. H. BISKIND and A. M. YOUNG. *West. J. Surg.*, **55**, 94–96, Feb. 1947. 4 figs., 2 refs.

455. **Final Observations on Congenital Defects in infants following infectious Diseases during Pregnancy, with Special Reference to Rubella.**

By C. SWAN, A. L. TOSTEVIN, and G. H. B. BLACK. *Med. J. Austral.*, **2**, 889–908, Dec. 28, 1946. 32 refs.

This paper records the results of a second study of 2 earlier series of cases of congenital defect in infants subsequent to maternal rubella in pregnancy and of the study of a fourth series of cases, and summarizes the results of the South Australian investigations carried out during the last 5 years. A table gives an analysis of the data obtained on re-examination of 61 children whose mothers had suffered from rubella in pregnancy. Details of the congenital defects present and of the physical development of these children are shown. Another table gives an analysis of type and period of onset of infectious disease during pregnancy and of the congenital defects in 25 infants born subsequently. The summary is based on the present and earlier papers. This records the congenital abnormalities found following rubella, morbilli, mumps, varicella, herpes zoster, scarlet fever, and influenza during pregnancy. Out of 154 infants whose mothers suffered from one or more of the above-mentioned diseases, 119 showed congenital malformations. In 3 further cases, congenital malformations occurred in the offspring in the absence of a history of maternal infection during pregnancy. These findings are discussed in detail. In this series only 3 out of 62 babies whose mothers had had rubella in the first 2 months of pregnancy were free from congenital abnormalities. Thus it is possible that rubella in early pregnancy is not invariably followed by congenital defects in the baby. Fox and Bortin have reported on an epidemic of rubella in Milwaukee during 1942–44. Eleven women suffered from the disease in the first 4 months of pregnancy. One mother was delivered of a stillborn hydrocephalic infant, and with one doubtful exception, in all of the remaining instances the babies born subsequently were normal. These diametrically opposed American findings may have been due to an error in diagnosis or to an alteration in virulence of the virus. No conclusive evidence is yet available with regard to the effect on the foetus of other infectious diseases during pregnancy.

J. M. Smellie

456. **Treatment of Premature Infants with Quinton's Serum.** (Sul trattamento dei prematuri con il plasma di Quinton. Studio di osservazioni cliniche di prematuri presso la clinica ostetrica di Ginevra.)

By G. PIANO. *Ginecologia*, **12**, 218–230, July-Aug. 1946. 6 figs., 16 refs.

In 1907 Quinton introduced his "serum" into postnatal therapy. Between 1938 and 1944 about 1,000 premature and debilitated infants were treated with this serum in the Geneva maternity hospital. The results obtained are described in this article. Quinton himself defines the preparation as "sea water of absolute purity, approximately isotonic to human plasma, sterilized without the use of boiling or of chemical agents, and

stored in sterile glass containers". One can prepare a practically isotonic solution by adding 5 parts of distilled water to 2 parts of sea water. In sterilization the method of choice is cold filtration, as sterilization by heat has numerous disadvantages. Some preparations are on the market under proprietary names. There are relations between the composition of sea water and that of the "vital milieu" of organisms; in the case of the vertebrates the blood plasma. Chemical elements are found in both in approximately the same percentage.

Parenteral administration of the sea water is to be preferred to oral use. The doses vary, according to weight and age of the patient, from 10 to 60 ml. The author gave subcutaneous injections of not more than 20 ml. a day. The serum should be warmed to body temperature. Properly prepared sea water has no toxic effects; it is possible to inject into dogs an amount of sea water equalling 60 per cent of their weight without any ill effects. The beneficial action of Quinton's serum is explained by increase of blood volume, acceleration of circulation, and increase of renal function. In addition to these physical factors the minerals have an important chemical function in the metabolism of the cells, tissues, and the whole organism. The foetus, particularly in the last months of its intrauterine life, selects those minerals which are of vital importance to its development. This explains the therapeutic value of the serum for infants who—owing to their prematurity (more correctly, immaturity)—suffer from a mineral deficiency.

For the evaluation of the clinical observations infants were classed as debilitated when signs of prematurity were missing, the weight was below 2,500 g., and the length below 50 cm. Infants with signs of prematurity were divided into three classes: (*a*) length at birth 40 to 44 cm.; (*b*) length at birth 44 to 46 cm.; (*c*) length at birth 46 to 48 cm. As most infants did not remain more than 10 days in hospital, the condition and weight of the infant on the tenth day were compared with those factors at birth. The results of the observations are as follows: 22.84 per cent had recovered their birth weight, 42.61 per cent had passed it, 32.82 per cent had not yet reached it, and 1.72 per cent had died. Two of these 9 infants died of cerebral haemorrhage. It should be pointed out that the hospital is not provided with incubators. In the normal infant the birth weight is usually regained between the eighth and twelfth days, but in the premature infant recovery of the birth weight is usually only achieved after weeks. In addition to these two curves the author adds the weight curves of the premature infants treated with serum, separate curves being given for classes (*a*), (*b*), and (*c*). Their course differs from that in the untreated premature infant and approaches that of the full-term baby. The descending phase is diminished, the rise earlier and regular. A sixth graph shows the curves of the normal and the premature infant, and the mean of curves (*a*), (*b*), and (*c*), all originating from a point which represents the weight at birth. From this it is obvious that the loss of weight in premature infants treated with serum is relatively even less than that of normal infants and that the birth weight is regained on the tenth day. The author believes that the addition of Quinton's serum to the usual therapeutic measures will improve the prognosis of prematurity.

Hilde Eisner.

457. **Measures for the Protection of Newborn Infants. I. Description of Measures Instituted in May 1937, at Long Island College Hospital.**

By C. A. Weymuller, A. C. Beck, and E. J. Ittner. *J. Amer. med. Ass.*, **133**, 78–84, Jan. 11, 1947. 11 figs., 2 refs.

The authors discuss measures employed since May, 1937, to control cross-infection among infants in the Maternity Unit of the Long Island College Hospital, Brooklyn, where 1,500 infants are cared for annually. Among circumstances favouring infection in nursery units are, unnecessary visiting, especially by children; overcrowding of infants in nurseries; assignment of nurses to duties which entail contact with a large number of infants; proximity of milk-room to nurseries, and return of unsterilized implements from nurseries to milk-room; proximity of isolation to uncontaminated units. Arrangements in the Brooklyn unit were designed to avoid these and other dangers.

Reduction of contacts was achieved as follows: (*a*) Visiting times to mothers were only 5 hours per week. Visitors wear masks and gowns and are separated from beds by rope barriers. (*b*) Throat cultures are made from nurses before duties are

begun; rejection occurs if possible pathogens are found. Masks and gowns are worn constantly in nurseries. (*c*) The physician enters the nursery only in emergency, and normally works in an examination room attached to each nursery unit (Fig. 1). Gown, mask, and gloves are worn, and are changed on moving to another nursery unit. House officers are confined to duties in a single unit. (*d*) Ward maids observe similar restrictions.

Drugs and diagnostic apparatus are duplicated in each nursery unit. Sterilized bedding and clothing are supplied daily to each nursery and placed beside individual beds. The layout of the nursery unit is carefully designed (Fig. 1). Although units are for 16 cribs, an 8 crib unit is considered better

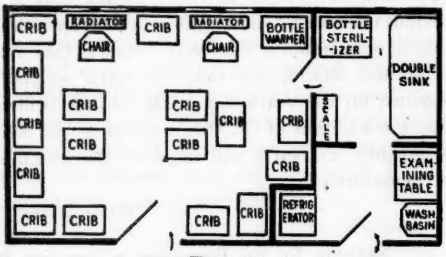

FIG. 1.

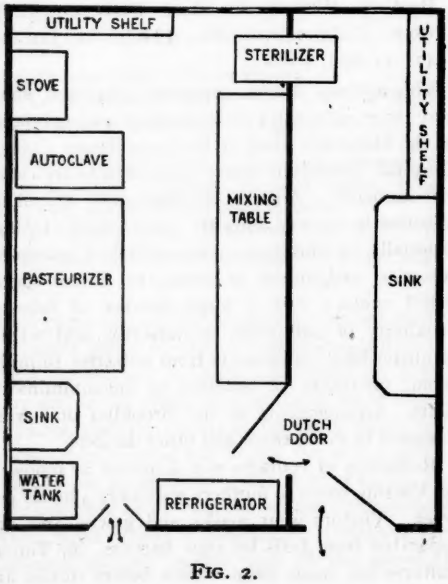

FIG. 2.

by the authors. Prevention of case to case contact by intermediaries is practised as follows: (*a*) One nurse cares wholly and solely for a group of 8 full-term babies and 1 premature baby. (*b*) The layout of the milk-room is shown in Fig. 2. It is distant from the nurseries. All material enters through a sterilizer in an anteroom. Sterile precautions are observed by nurses working in the milk-room; nurses are withdrawn if they develop any infection. Milk mixtures are pasteurized (140° to 160°F. (60° to 71°C.) for 30 minutes) after preparation. Before return to the milk-room utensils are sterilized in the nursery. Sterile milk mixtures are taken to the refrigerator in each nursery unit in a closed cart. The "utility room" commonly attached to nurseries is eliminated. (*c*) An isolation unit, distant from the nurseries, is provided for infants suspected of infection, and sick infants are rigidly isolated in the separate paediatric section.

Skin infections are reduced by routine prophylactic anointing of each infant soon after birth with 15 g. of 5 per cent sulphathiazole ointment, repeated if any contact occurs with infection. By this measure the incidence of pyodermia was reduced to 0.9 per cent from a previous level of 16 per cent. If an infection develops in a nursery unit, the affected infant is isolated and the contaminated unit is closed to all admission until risk of further infection is over, and when empty is scrubbed with soap and water, no admission being permitted for a full 24 hours thereafter.

The good results ensuing from this prophylactic technique are considered, and the methods of control of an epidemic of diarrhoea which followed a breakdown of the technique due to wartime shortage of nurses are described. During the epidemic it was established that if the technique outlined above is followed closely (*a*) a common milk-room for all infants, sick or well, can be used without risk of cross-infection, and (*b*) a clean nursery can, without cross-infection, be operated beside one contaminated with neonatal diarrhoea.

M. MacGregor

458. **Epidemic Diarrhea in the Newborn. The relation between Breast and Bottle Feeding and the Early Development of the Proper Intestinal Flora.**
By H. W. MAYES. *Amer J. Obstet. Gynec.*, 53, 285–289, Feb. 1947. 3 refs.

459. **Bacteriology of the Oronasal Cavity of the Newborn.**

By J. L. CORNELISON, E. A. JOHNSON, and W. M. FISHER. *Amer. J. Obstet. Gynec.*, **52**, 797–802, Nov., 1946. 6 refs.

Two groups of new-born babies were studied. In the first group, consisting of 100 unselected new-born infants, an attempt was made by the use of selective media to isolate staphylococci, coliform bacilli, and moniliae from the oronasal pharynx and nasal orifices. The second group of 50 unselected new-born infants was studied with special reference to streptococci and pneumococci. The bacteriological results were correlated with the type of delivery and length of time of rupture of the membranes.

There were no staphylococci, coliform bacilli, or moniliae in 39 of the 100 cultures in the first series; 21 plates were positive for coliform organisms, and of these 11 showed the cultural characteristics of *Bacterium coli*. Yeast strains were isolated in 11 cases but only 2 were *Candida albicans*. Forty-four strains of haemolytic staphylococci were isolated, 2 of which were coagulase-positive. The longer the membranes were ruptured before delivery the higher was the percentage of positive cultures. Positive cultures for staphylococci, coliform bacilli, or moniliae were obtained in 64 per cent of the infants delivered spontaneously and in 61 per cent of those delivered by low forceps. Two infants delivered by mid-cavity forceps gave positive cultures for staphylococci, but 2 delivered by Caesarean section were negative for the three organisms studied.

Pneumococci were not found by the methods used in the second group of unselected new-born infants, but α-streptococci were found in 6 cases and β-streptococci in 4. The fact that both strains of streptococci grew at 45°C. and were not killed by heating for 30 minutes at 60°C. indicated that they belonged to the enterococcus group. There was a larger percentage of β-streptococci present when the membranes had been ruptured a long time or when forceps had been used.

T. N. MacGregor

460. **The Problem of the Suckling.** (Zum Stillproblem.)

By W. R. MERZ. *Schweiz. med. Wschr.*, **76**, 1177–1179, Nov. 16, 1946. 2 figs., 24 refs.

Statistics for breast feeding in Switzerland are presented. During the last 20 years the rate has remained stationary and unsatisfactory in spite of continuous propaganda and the award of certain benefits to mothers who breast-feed their infants. At the end of the tenth week the rate was approximately 55 per cent. The negative attitude of the mothers and the relative inactivity of the maternity hospitals in combating this attitude, probably due to lack of well-trained nursing staff, are regarded as the principal causes of this position. A table compares the breast-feeding rate at the time the mother is discharged at several Swiss hospitals for a period of 11 years (1934–44). The figures vary considerably (from 46.4 to 83.5 per cent). The suckling ability of 2,400 healthy mothers with healthy babies was checked during the first 10 days after birth, the decisive period for the initiation of breast feeding. Three groups are distinguished: total breast feeding, partial breast feeding, and artificial feeding. In the first group all mothers were included who could satisfy the individual requirements of the infant. The mutual relations of these groups are charted. The typical increase of the breast-feeding incidence during the first 3 to 4 days and the sudden decline on the sixth and seventh days are demonstrated and the principal causes explained. On discharge only about 50 per cent of the mothers (54 per cent on the ninth and 52 per cent on the 10th day) were wholly breast feeding, an unsatisfactory rate. The problem of hormonal relationship between the mother's suckling ability and the engorgement of the breasts in the new-born was studied in 450 cases. The group of mothers who were partially breast feeding on the ninth or tenth day (41 per cent) was subdivided according to degree of suckling ability. The result was inconclusive. No correlation between the incidence and degree of engorgement, and suckling ability could be found.

A short survey of measures, old and new, for promoting the ability to breast feed includes general rules for the pregnant woman, for drug treatment, for the care of the breasts during the onset of lactation, and for the prevention of complications during labour and the puerperium. Incidentally, mastitis has the least influence of all complications on the suckling ability. The maxim is accepted that "a bad conduct of breast

feeding has a greater bearing on infant mortality than a bad conduct of labour."

[The figures for England and Wales for the years 1931–41 indicate a decline in initial incidence of breast feeding of 5.6 per cent. About 80 per cent of the babies leave the hospital wholly breast fed. At the end of the third month the rate is 50 per per cent. The most effective measures to promote breast feeding are the utmost restraint in the introduction of complementary feeding, complete emptying of the breasts after each feed, and adequate nutrition of the mother. Thus a breast-feeding rate of 98 to 99 per cent can be achieved.]

M. Dynski-Klein

461. **Causes of Stillbirth.** (Neonatale sterte en haar oorzaken.)

By F. Willemijns. *Belg. Tijdschr. Geneesk.*, **3**, 301–316, Apr. 1947. 3 figs.

462. **Studies in Infant Mortality. Part II. Social Aetiology of Stillbirths and Infant Deaths in County Boroughs of England and Wales.**

By B. Woolf. *Brit. J. soc. Med.*, **1**, 73–125, April 1947. 6 figs., 17 refs.

This is a very important contribution to our knowledge of the aetiology of stillbirths and infant deaths; it is a sequel to a previous paper by Woolf and Waterhouse (*J. Hyg. Camb.*, 1945, **44**, 67). The earlier article contained statistical tests showing the social and medical reasons for regarding the relation between infant mortality and the social variables as a real one, in the sense that improvements in social conditions might be expected to reduce infant deaths. But it did not deal with the questions of social aetiology; of how overcrowding, low earnings, and so on exert their influence on the life of the baby. This further aetiological analysis, however, is carried out in the present paper and regression equations are given for the separate diagnostic groups and age periods during which death occurs. It also deals with stillbirths.

In the first paper, for the 11 years 1928–38 inclusive, the average equation was $M=23.1+0.51H+0.46U+0.29P+0.35F+2.01L$, where the indices used were:

H = Percentage of families with more than 1 person per room.

U = Average monthly percentage unemployment amongst adult males.

P = percentage of occupied males in social classes IV (semi-skilled) and V (unskilled workers).

F = Percentage of females aged 14 years and over employed in manufacture.

L = Degree of latitude north of 50° 30′.

In the present paper an index expressing size of family (G) and one expressing local density of population (D) have been added. A regression constant (K) is also used to denote an estimate of infant mortality rate if adverse social conditions are excluded. The author deals with infant mortalities as a whole for different social grades according to individual cause and for different administrative areas. Congenital causes showed little variation according to social grading. Class V being to Class I in the ratio 1.5 to 1; but for pneumonia and bronchitis the ratio of Class V to Class I was 6.75 to 1, for infectious diseases 5.4 to 1, and for diarrhoea 4 to 1. Regarding areas, county boroughs had a total infant mortality rate of 70.8—12 units higher than for urban districts and London and 16 higher than for rural districts. Among individual diseases, London had a higher diarrhoea rate than county boroughs, but London had by far the lowest figure for congenital defects. Woolf deals largely with the rates for county boroughs, and in a table the regression equations are given for 82 of them for the 11 years 1928–38. Another table shows how infant mortality and stillbirth-rates are associated with various social conditions; the different grouped causes of infant mortality; and the period in the year of a child's life in which death occurred.

Mortality rates associated with social indices grouped into aetiological categories are also tabulated.

The aetiological conclusions that would seem to follow from these figures are stated and discussed. They include the following: (*a*) Poverty (probably mainly malnutrition) and crowding are of approximately equal importance in infant mortality. Crowding is relatively unimportant in stillbirth rates, whereas poverty has a very big effect. For the combined rate, therefore, poverty is much the more influential, making an estimated contribution of about 37 as against 10.5 attributable to crowding. (*b*) At equal degrees of crowding and poverty, stillbirth and neonatal-death rates de-

crease with increasing size of family. This is in line with the fact that first births are known to carry an excess risk in these categories of mortality. In postnatal deaths and in all the zymotic-cause groups, larger families involve higher rates, because of the increased risk of infection of the baby by its elder sibs. (*c*) For the infectious diseases, bronchitis, and pneumonia groups, mortality increases with increased crowding (exposure to infection) and poverty (lessening of resistance). In diarrhoea, mortality increases with crowding, but at equal degrees of crowding seems to be greater for the better-off than for the poor. This is in line with the high diarrhoea rate in London. (*d*) Stillbirths and neonatal mortality tend to be lower in more densely populated and larger conurbations than in smaller communities. This is also in line with the comparative figures for London, and is attributed to the better social and medical care available in the larger places. (*e*) The disparity between well-off and poor is much greater in postnatal death rates, in which bad social conditions and large family size both act to increase mortality, than in stillbirths and neonatal deaths, where poverty and large family size act in opposite directions. (*f*) The effect of latitude is so distributed that it appears to be an expression of influences acting on the child at birth through the mother. (*g*) Industrial employment of women seems to be associated with increases in all categories of mortality. (*h*) The larger the family size the higher the mortality rate among live-born infants. But large family size decreases the stillbirth rate so much that it more than cancels the increase in infant mortality. If the reproductive rate could be increased, other social conditions being unchanged, then a decrease would be expected rather than an increase in the rate of wastage of infant life.

The fall in stillbirth and infant mortality rates from the 1938 level during the war period is of the order of magnitude to be expected from the levelling up of nutritional standards among the worst-off section of the population. The estimated mortality rate (infant mortality plus stillbirths) in the "crowded poor" section of the population of county boroughs is computed as about 136, and of the "unemployed crowded poor" as about 232. The latter figure is more than twice the mean rate. Detailed comparisons are given between computed rates at these social levels and that of the "better-off" section of the community. The scope and limitations of the multiple regression method are discussed, and the need for field research is emphasized.

E. H. M. Milligan

Rh factor, erythroblastosis foetalis.

463. **Review of Cases of Rh Iso-immunization during the Past Five Years in the Royal Victoria Montreal Maternity Hospital.**

By N. W. PHILPOTT, J. P. A. LATOUR, and G. J. E. VAN DORSSER. *Amer. J. Obstet. Gynec.*, **52**, 926–937, Dec., 1946. 23 refs.

This paper reviews a total of 12,114 obstetric cases delivered in the 5-year period ending Dec. 31, 1945. There were 30 cases of haemolytic disease of the newborn—that is, 1 in every 404 deliveries. Of the 30 infants, 19 were born alive but 6 died before leaving hospital. Eleven of the remaining 13 have been followed up, and of these 8 are normal, and 3 are mentally retarded and have residual spasticity. Seven of the 30 pregnancies were interrupted at the thirty-sixth week, 5 by Caesarean section and 2 by other methods. This resulted in 4 live births and 3 stillbirths; only 1 of the 4 live infants survived. From the full-time pregnancies there were 15 live births and 8 stillbirths. Thus premature interruption did not yield good results. Among the 30 cases there were 4 of toxaemia, an incidence that is not significantly higher than that found in pregnancies not productive of haemolytic disease. Nor was there any case of retroplacental haemorrhage, which has been claimed to be more frequent in cases of Rh iso-immunization.

In the Royal Victorial Hospital, Montreal, all obstetric patients are tested for the Rh factor. If the patient is Rh-negative, her husband's type is determined. If this seems indicated, Rh-negative women are tested for antibodies at the third, sixth, and eighth month. If antibodies are present the type and titre are determined, and the titration is repeated each month. When the antibody titre increases to 1 in 100 this is taken as an indication of the foetal involvement, especially if the history denotes previous foetal mishaps. In 7 cases pregnancy was terminated at the thirty-sixth week for the purpose of lessening the damage to the foetus. If the husband is heterozygous and

the history shows repeated foetal mishaps, contraceptives are indicated or even ligation of the tubes.

Early diagnosis is essential in the adequate treatment of the affected baby. The infants of all Rh-negative mothers, whether the latter exhibited antepartum antibodies or not, are typed for the Rh factor immediately after delivery. In this group daily haemoglobin estimations are done on all Rh-positive babies during their stay in hospital. If the haemoglobin is below 90 per cent at birth or if the daily fall is more than normal, repeated small transfusions are given (10 ml. per lb.: 22 ml. per kilo) of Rh-negative blood. Mothers' milk is not given, as it has been shown to contain Rh antibodies.

F. J. Browne

464. **The Antepartum Prediction of Hemolytic Disease of the Newborn.**

By E. W. PAGE, M. HUNT, and S. P. LUCIA. *Amer. J. Obstet. Gynec.*, **52**, 794–796, Nov. 1946. 1 ref.

As the obstetrician is unable to forecast the outcome of the pregnancy in an Rh-negative mother, the present study was undertaken in the hope of formulating some guiding principle. The material for the study was selected from 4,000 pregnant women seen in the obstetric clinic of the University of California Hospital and in the private practices of six obstetricians. The blood serum of each patient was tested for agglutinating antibodies against two Rh-negative, group O, and two Rh-positive, group O, red blood corpuscle suspensions. Wiener's method was used for the detection of blocking antibodies.

It was apparent from a study of 26 cases, in which the time of appearance of the antibodies could be fixed, that when the antepartum duration of antibodies was 10 weeks or less erythroblastosis did not occur. Forty-nine cases were analyzed in which antibodies were detected in the blood more than 11 weeks before delivery. In 19 of these, traces only of either agglutinating or blocking antibodies were found. One case in this group developed a possible erythroblastosis foetalis—the child had a slight increase in nucleated red cells associated with a mild anaemia at birth. Appreciable amounts of antibodies or small amounts on repeated occasions were found in 30 cases. In 22 of these, antibodies appeared more than 10 weeks before delivery and in this group there were 16 cases of erythroblastosis foetalis; the remaining 6 women were delivered of healthy infants, 4 of whom were Rh-negative. Further analysis of the figures showed that all the mild cases of erythroblastosis foetalis occurred in the 10 to 14-week group, while all the severe cases, including 7 of fatal hydrops foetalis, were in the group in which maternal antibodies had appeared at least 15 weeks or more before delivery.

The suggestions the authors make from this preliminary study are: (1) All pregnant women should be routinely typed and in all Rh-negative patients with Rh-positive husbands the blood should be examined for antibodies not later than the twenty-fourth week of gestation. (2) If the blood is strongly positive for either agglutinating or blocking antibodies, nothing need be done, as an Rh-positive foetus will be too seriously affected, while an Rh-negative foetus will escape the disease. (3) If antibodies are present only in traces or the presence of a small amount is not confirmed, the foetus is probably unaffected and it is unwise to interfere. (4) If no antibodies are found initially but a significant amount appears later, 8 to 10 weeks may be allowed to elapse before haemolytic disease becomes probable. Labour may be induced after this time provided it is within 6 weeks of term.

T. N. MacGregor

465. **Kernicterus in Erythroblastosis Foetalis.**

By V. C. VAUGHAN. *J. Pediat.*, **29**, 462–473, Oct. 1946. 27 refs.

Seventy-four cases of erythroblastosis foetalis have been diagnosed at the New Haven Hospital, Connecticut, in 17 years. There have been 27 deaths and 23 necropsies have been performed. A clinical account is given of the signs and symptoms preceding the death in 13 of the fatal cases, all of which were found at necropsy to have kernicterus. The specificity of opisthotonos and rigidity as signs of kernicterus was suggested by the fact that 4 survivors who showed these symptoms were mentally retarded and had some motor disability. The author finds a relationship between the occurrence of kernicterus and the severity of blood destruction, as measured by blood counts, by size of spleen, or by depth of jaundice. The time of

onset of icterus seemed to have no prognostic significance in this series. Kernicterus was found somewhat more commonly in the smaller babies, but the author claims no statistical significance for this observation.

The relation of transfusion to prognosis in erythroblastosis is considered. "It is seen that no infant who received Rh-positive blood on the first day of life died with kernicterus. This suggested superiority of Rh-positive blood . . . in preventing kernicterus is by no means statistically significant, but it represents the most striking deviation from the general finding that the type of blood used in therapy had no affect on the outcome." A discussion follows on the possible mechanism of production of the lesions of kernicterus. Early investigators of the Rh factor were unable to demonstrate it in cells other than the red blood cells. It now seems probable that the Rh factor is a general characteristic of tissue cells. But whether kernicterus represents a primary nerve-cell injury or primarily a vascular injury is still unknown. The possible role of "blocking antibody" in moderating blood-cell destruction is discussed, as is the use of Rh-positive blood transfusion to "mop up" circulating antibody.

A Doyne-Bell

466. **Hemolytic Disease of the Newborn (Erythroblastosis fetalis). Treatment by a Single Massive Transfusion, with Complete Recovery.**

By A. BLOXSOM. *Amer. J. Dis. Child.*, 72, 320–324, Sept., 1946. 10 refs.

An infant with icterus gravis neonatorum was given a transfusion with 90 ml. Rh-negative blood and 50 ml. of plasma during the few hours following birth. The next morning it was given a further transfusion and, owing to an accident, received 310 ml. of blood in a short space of time. The infant became red and perspired freely but showed no other untoward effects. Whereas before the transfusion the infant's "reaction for the Rh factor" was only weakly positive, 10 days later it had become strongly positive. The author concludes that the transfusion supplied some "undoubted anti-antigen-antibody factor."

[There is no need to postulate any unknown factor to explain weakly positive Rh reactions in infants with icterus gravis. It has been shown that the red cells of such infants are coated with anti-Rh antibody which sometimes makes them difficult to agglutinate. In time the supply of antibody is used up and the red cells then agglutinate more strongly.]

P. L. Mollison

OBSTETRIC OPERATIONS

467. **The Place of Caesarean Section in Modern Obstetrics.**

By J. BARNES. *Postgrad. med. J.*, 23, 157–161, Mar. 1947. 4 refs.

468. **Cesarean Section.**

By A. W. ANDISON. *Canad. med. Ass. J.*, 56, 170–177, Feb. 1947.

469. **Sulfonamides as a Prophylactic Agent in Conjunction with Cesarean Section.**

By H. C. HESSELTINE and C. THELEN. *Amer. J. Obstet. Gynec.*, 52, 813–816, Nov. 1946. 4 refs.

The authors state that from their observations "it is evident that the use of sulfonamide locally did not lower the morbidity rate or shorten convalescence. Furthermore, the bladder peritoneum seemed more adherent in a few patients subjected to laparotomy subsequently. This may not be serious, but it requires greater caution in the reflection of this tissue in subsequent laparotrachelotomies. Therefore, the local deposition of sulfonamides, either within the uterine cavity or over the uterine incision (but under the peritoneal reflection) did not reveal any prophylactic value. It did increase adhesions of the peritoneum to the uterus. There exist also the dangers of drug sensitization.

"The sulfonamides in relation to Cesarean section should be used on direct indication in relation to a proper bacteriologic study of the uterine cavity and blood stream, except in such urgent situations where the withholding of the drug would jeopardize the patient's convalescence or life. Even in this event, to-day penicillin would seem preferable to the sulfonamides with but few exceptions. Penicillin, like any other medicament, should be employed in sufficient and proper dosage and only when properly indicated."

470. **Abdominal Drainage in Caesarean Section for Infected Cases.** (El drenaje abdominal en la operación cesárea del caso impuro.)

By A. PERALTA RAMOS. *Prensa méd. argent.*, 34, 343–349, Feb. 21, 1947.

471. ***d*-Tubocurarine in Caesarean Section.**

By T. C. GRAY. *Brit. med. J.*, **1**, 444-445, Apr. 5, 1947. 3 refs.

A series of 30 cases in which curare has been used for Caesarean section is reported. Premedication consists of atropine gr. $\frac{1}{100}$ (0.65 mg.) given 1 hour beforehand; when the surgeon is ready the induction is carried out on the table with 15 mg. of *d*-tubocurarine ("tubarine") given intravenously, followed by 0.3 g. of "kemithal" in a 5 per cent solution. Anaesthesia is maintained with cyclopropane in a closed circuit, and respiration is "aided" so that no sub-oxygenation may result from the slight depression of respiration that may occur. Light anaesthesia is maintained until the time of delivery, after which it may be deepened. To build up the carbon dioxide tension in the blood of the foetus and so encourage its initial respirations on delivery, the soda-lime container is cut out of the circuit for a few minutes before the uterus is incised. It is inadvisable to use a pharyngeal airway as it may cause vomiting and retching.

The results are considered encouraging, only 2 of the babies having failed to cry immediately; one of these had received thiopentone instead of kemithal and the other was premature (32 weeks) with an eclamptic mother; both cried after a short period. There was increased contractility of the uterus and the placenta separated easily; post-operative vomiting and chest complications were minimal; there was no retention of urine, and eye symptoms and ileus were absent. Prostigmine was necessary in 2 cases.

The author considers that this form of anaesthesia fulfils the following criteria: it is safe and pleasant, provides good working conditions for the surgeon, and is not depressing to the child and to the uterine tone. Many of the cases in this series were admitted as emergencies with a consequently increased liability to vomiting during the induction. It is thought that the use of curare not only reduces this liability, but also greatly facilitates intubation should it become necessary. The freedom from curarization of the child is in accordance with the findings of Whitacre and Fisher (*Anaesthesiology*, 1945, **6**, 124), and the substitution of kemithal for thiopentone is considered important. In all cases convalescence was uneventful.

[The degree of placental transmissibility of curare has not yet been fully established. Until such time, this method should be used only by experts, and even then only when all the facilities for maternal and foetal resuscitation are at hand. The theoretical possibility of causing premature respirations in the foetus should also be kept in mind when following the practice of building up the maternal carbon dioxide tension shortly before delivery. Good results for "myanesin" in Caesarean section are claimed by Mallinson (*Lancet*, 1947, **1**, 98).]

G. C. Steel

472. **Postmortem Cesarean Section.**

By R. O. JOHNSON and T. V. FRANK. *Amer. J. Obstet. Gynec.*, **53**, 343-344, Feb. 1947. 9 refs.

473. **The Selection of Forceps for Midpelvic Arrest of the Vertex.**

By L. LANGMAN and H. C. TAYLOR. *Amer. J. Obstet. Gynec.*, **52**, 773-782, Nov. 1946. 25 refs.

The management of mid-cavity arrest of the vertex has always been a difficult obstetric problem and one which has not been studied statistically. There is no general agreement as to the best type of forceps to use for the delivery of the vertex delayed or arrested in the mid-pelvis. Some believe that once the accoucheur is familiar with one type of forceps he becomes so dexterous with it that he can use it to the exclusion of all other types in every case necessitating forceps delivery; others consider that one type of forceps is not suitable for every case, and that instruments should be available and used according to each particular problem. It has been the practice in the Bellevue Hospital Obstetrical Service, New York, in recent years for the operator to select the type of forceps according to the particular position of the occiput and the architecture of the pelvis. Three types of forceps have been used—the classical (most commonly Haigh-Ferguson), the Barton, and the Kielland.

The material in this study consisted of 701 mid-cavity forceps operations occurring among 10,814 deliveries in the Bellevue Hospital Obstetric Service between Jan. 1, 1934, and Dec. 31, 1945. The factors which influenced the selection of forceps were the experience of the operator with one special type, the position of the occiput, the type of pelvis, and the size of the foetus. When the occiput was anterior the classical forceps was used almost exclusively in the Bellevue Service. In transverse positions of the occiput 75 per cent of

cases were delivered with the Barton forceps, while in 50 per cent of posterior positions of the occiput the Kielland forceps was employed. The Barton forceps became so popular in the Bellevue Service that often posterior positions of the occiput were manually rotated into the transverse or oblique so that this type might be used in preference to the Kielland forceps. As there is a tendency for posterior and transverse positions of the occiput to persist in android and anthropoid pelves, the Barton and Kielland forceps were used predominantly for such cases. The Kielland forceps proved more unsuitable than the others when the foetus was large.

There were 4 maternal deaths in the series of 701 cases, and 3 of these were attributed to the type of delivery, giving a maternal mortality rate of 0.4 per cent for mid-pelvic forceps delivery. The morbidity rate for the series was 41.3 per cent, the standard of morbidity being a rise of temperature to 100.4° F. (38° C.) on at least one occasion on 2 separate days postpartum. The lowest incidence of morbidity was in the group delivered by Haigh-Ferguson forceps.

Type of forceps first applied		Type of forceps with which delivery was completed		
		Classical total cases	Barton total cases	Kielland total cases
Classical	211	183	24	4
Barton	357	30	314	13
Kielland	132	18	9	104

Trauma to the birth canal was most marked when Kielland and Barton forceps were used; 3 vesico-vaginal fistulae, all of which closed spontaneously, were associated with delivery by the Barton forceps. The total foetal mortality, stillborn and neonatal, for the whole series was 9.4 per cent, but the mortality directly attributable to the forceps operation was 5.2 per cent. The foetal mortality associated with Kielland forceps was almost three times greater than that for the Barton and the classical forceps, but the Kielland forceps was preferred in the greater proportion of posterior positions and was employed when one of the other types had been applied unsuccessfully. Delivery was not always possible by the type of forceps first applied, as is seen in the table.

T. N. MacGregor

See also No. 443

MISCELLANEOUS

474. **The Trend of Modern Obstetrics.**
By E. A. KEELAN. *Irish. J. med. Sci.*, 55–63, Feb. 1947.

475. **A Review of 9,000 Obstetrical Cases at the Harris Memorial Methodist Hospital, Fort Worth, Texas.**
By G. H. BEAVERS, J. BENNETT, R. L. GROGAN, and C. HIETT. *Tex. St. J. Med.*, **42**, 640–645, Mar. 1947.

GYNAECOLOGY

476. **Gynaecology in the Women's Services.**
By J. MOORE. *Lond.* (*Roy. Free Hosp.*) *Sch. Med. Mag.*, **8**, 37–41, July-Sept. 1946.

477. **Pelvic Examination for Nurses.**
By E. ALLEN and C. GALLOWAY. *Amer. J. Obstet. Gynec.*, **53**, 290–295, Feb. 1947. 14 refs.

478. **Radium and X-rays in the Treatment of Diseases of Women.**
By W. T. DINGLE. *Manitoba med. Rev.*, **27**, 144–146, Mar. 1947.

479. **Study of Some Functional Aspects of Conservative Gynaecology.** (Estudio sobre algunos aspectos funcionales de la ginecologia conservadora.)
By W. KOCK. *Bol. Soc. chil. Obstet. Ginec.*, **11**, 185-203, Oct., 1946. 14 figs., 14 refs.

480. **Effect of Oestradiolbenzoate and Diethylstilboestralpropionate on the Uterus.**
(Uber die Wirksamkeit von Ostradiolbenzoat Diäthylstilböstraldipropionat auf den Uterus.)
By E. HUF. *Dtsch. med. Wchsr.*, **72**, 84–85, Feb. 14, 1947. 8 refs.

481. **Testoviron Implantation in Gynaecology.** (Implantace testovironu v gynaekologii.)
By O. VALENTA. *Ceskoslov. Gynaek.*, **12**, 36–48, 1947.

482. **Dienestrol. Another Synthetic Estrogen of Clinical Value.**
By S. H. SIKKEMA and E. L. SEVRINGHAUS. *Amer. J. Med.*, **2**, 251–252, Mar. 1947. 5 refs.

Menstrual Disorders.

483. **Control of Menstrual Disturbances and Hypo-ovarian Sterility. Nine Years of Experience with Equine Gonadotropin.**
By G. J. HALL. *Amer. J. Obstet. Gynec.*, **53**, 259–262, Feb. 1947. 4 refs.

484. **Dysmenorrhoea.**
By DEWITT D. PHILLIPS. *J. Bowman Gray Sch. Med.*, **5**, 27–32, Jan. 1947. 36 refs.

485. **Edrisal in the Management of Dysmenorrhea.**
By C. F. LONG. *Industr. Med.*, **15**, 679–681, Dec. 1946. 5 refs.

"Edrisal" is a tablet containing acetylsalicylic acid gr. 2½ (0.16g.), phenacetin gr. 2½ (0.16 g.), and amphetamine sulphate gr. 1/26 (2.5 mg.). Incorporation of amphetamine overcomes depression and nervous tension which frequently accompany menstruation and, in addition, provides mild analgesia. In a series of 630 women treated with edrisal throughout 1 year, 90 per cent got the relief they sought and lost no time from work.

D. Stewart

486. **Dysmenorrhea in Industry—Treatment with a New Antispasmodic.**
By F. A. VIGGIANO. *Industr. Med.*, **15**, 632–635, Nov. 1946. 17 refs.

A total of 221 patients was treated for dysmenorrhea with "pavatrine", a comparatively new antispasmodic whose chemical formula is beta-diethylaminoethyl-fluorene-9-carboxylate hydrochloride. It is emphasized that, owing to restrictions placed on the industrial physician, gynaecological examination was not permitted, and the treatment was, of necessity, purely symptomatic. Of the patients 19 were treated during two successive menstrual periods, 1 was treated twice with an interval of 3 days, and 1 during three successive periods, giving a total of 243 courses of treatment. A single dose of two pavatrine tablets (0.25 g. or 4 gr.) was given, followed by a glass of warm water and 1 hour of rest in bed; 76.6 per cent of the patients were able to resume work in 1 hour, 12.7 per cent obtained slight relief and were able to resume work during the same day, while the remaining 10.7 per cent had no relief and were referred to their own physicians for gynaecological examination. These figures compare favourably with those obtained in 128 other patients to whom another antispasmodic was given; only 64 per cent of the latter were able to return to work within 1 hour. The author concludes that pavatrine alleviates dysmenorrheic pains promptly in a high percentage of cases, and that this is of particular importance in the management of dysmenorrhoea in industrial workers.

[The author considers the number of patients sufficient to draw accurate conclusions. There may not be general agreement on this point, as the majority of patients were seen on only one occasion and without any classification of severity of pain.]

A. Lloyd Potter

487. **Surgical Treatment of Dysmenorrhea.**
By C. J. DUNCAN. *N. Y. St. J. Med.*, **46**, 2757–2759, Dec. 15, 1946. 1 ref.

The scope of dilatation and curettage of the uterus and of presacral neurectomy in the treatment of primary dysmenorrhoea is discussed, the author basing his experience on a series of cases at the Brookline Hospital for Women. He favours dilatation and curettage for mild cases and this in conjunction with presacral neurectomy for more serious cases. His operative technique for the latter is the standard one, but a ventro-suspension is done as well [it is not clear whether this is a routine or is performed only in indicated cases]. Sympathectomy gave total relief in 86 per cent in the series of 53 operations [a very high cure rate not always attained]. Secondary dysmenorrhoea usually needs surgical treatment of the pathological lesions present. Radical procedures were favoured in these cases. Presacral neurectomy in this group relieved only 30 per cent of patients.

R. K. Bowes

488. **An Evaluation of Presacral Neurectomy in the Treatment of Dysmenorrhea.**
By A. W. TUCKER. *Amer. J. Obstet. Gynec.*, **53**, 226–232, Feb. 1947. 7 refs.

The operation of presacral sympathectomy has been performed 420 times in the last 14 years at the Free Hospital for Women, Brookline. The author has followed up 255 of these cases in an attempt to assess the value of this operative procedure. Complete relief was obtained in 78 per cent of cases with essential dysmenorrhea and in 33.3 per cent of cases of acquired dysmenorrhea. These results do not give an accurate assessment of the value of presacral sympathectomy, as the author states that "in most cases the operation was routinely combined with a dilatation and curettage, a suspension and any other necessary pelvic surgery which the gynaecologic situation demanded."

Gladys Dodds

489. **A Case of Haematometria of Surgical Origin.** (Un caso de hematometria de origin quirúrgico.)

By J. A. CARRENO. *Med. Cirug.*, **11**, 116–121, Jan. 1947.

490. **Effect of Pregneninolone on the Menstrual Cycle of Adolescent Girls with Oligomenorrhea or Amenorrhea.**

By F. E. HARDING. *Amer. J. Obstet. Gynec.*, **53**, 279–284, Feb. 1947. 21 refs.

Zondek and Rozin suggested that in many cases of secondary amenorrhoea it is possible to produce "menstruation" by the use of luteinizing substances injected or taken by mouth. The underlying theory is that many of these patients have already enough oestrogenic hormones circulating. The author has used the oral method with "pregneninolone" (anhydrohydroxyprogesterone) in 46 girls between the ages of 11 and 19 years. In 5 with primary amenorrhoea the treatment failed completely, as was to be expected. The others had suffered from irregular menstruation and before treatment had varying histories of amenorrhoea.

Pregneninolone was administered in doses of 5 to 15 mg. daily by mouth. For irregular menstruation it was given from the eighteenth day of the cycle until the period started. In patients with amenorrhoea treatment was for 10 days each month or continuously till menstruation began. Of patients with amenorrhoea of 3 months' duration or less 87 per cent were improved. The method is not recommended where the interval is longer than 6 months. In general, 40 per cent of the patients continued to menstruate regularly during 6 months after cessation of treatment. In some 70 per cent who also had dysmenorrhoea the condition was relieved.

[It is always difficult to assess the value of reports on the treatment of amenorrhoea. So many factors are involved that treatment verges on the empirical. The results with luteinizing substances do not seem to differ much from those obtained by other methods.]

Kenneth Bowes

491. **The Treatment of Amenorrhea and Sterility by X-ray Therapy.**

By I. I. KAPLAN. *N. Y. St. J. Med.*, **46**, 2746–2752, Dec. 15, 1946. 34 refs.

The author is interested in the radiological treatment of patients who have difficulty in conception and who suffer from amenorrhoea. He now reports the results of 296 cases treated during 1925-45 and gives more details of the 117 cases seen between 1939 and 1945. The reason for success of this treatment is not fully understood. A disturbance in the balance between the ovaries, the pituitary, the uterus, and the thyroid is postulated, and the X-rays may act on the persisting corpus luteum. There is also evidence that irradiation of the ovaries may influence thyroid action. It is questionable whether irradiation of the pituitary stimulates or not.

High voltage X-rays were used (200 kV. and 10 mA. with 0.5 mm. copper and 1 mm. aluminium filters at 50 cm. distance). Anterior and posterior, right and left pelvic fields were used with 8 × 10 cm. or 12 × 15 cm. portals. The dosage was 50 to 75 *r* per treatment, given at weekly intervals for 3 weeks. All the patients had irradiation of the ovaries and most of them of the pituitary as well. There had been a gynaecological examination to exclude pelvic abnormalities [the extent of this investigation is not fully stated]. Out of 117 cases treated, 101 were followed up. Eighty-eight patients menstruated regularly; 38 became pregnant, 27 of the pregnancies resulting in normal babies; 3 miscarried; 1 had an ectopic gestation; and 6 were still pregnant.

[This is an interesting paper on a debatable subject. Unfortunately neither the statistics nor the clinical details are made very clear, as two overlapping series of patients are quoted.]

R. K. Bowes

492. **Amenorrhoea in the Ghetto.** (Die Ghetto-amenorrhoe.)

By J. NOCHIMOWSKI. *Med. Klinik.*, **41**, 347–348, Aug. 1946. 2 refs.

When Kovno was overrun by the Germans 30,000 Jews were shut up in the Ghetto at once. Among a number of the females there was a sudden cessation of the menses [the incidence is not given], to which the author gives the name "Ghetto-amenorrhoea." The usual physical concomitants of prolonged amenorrhoea were not seen, nor was there an increase of weight in the subjects. Pregnancy occasionally occurred. Libido was at first diminished, but was later greatly increased. Nothing abnormal was found on physical examination. After about nine months, when the community had more or less adapted itself to its altered

living conditions, menstruation began again with dramatic suddenness and intensity. Haemorrhage was profuse, lasting for a week, and was accompanied by intense pain in the abdomen and back. Subsequent menses were normal, and the women felt well and sometimes found that previous menstrual disturbances had now vanished.

The theory is advanced that the acute psychic trauma led to an overaction of the thyroid (hyperthyroidism was often seen in the Ghetto), that this caused a compensatory increase in production of follicular hormone, and that with the passing away of the psychic trauma and the consequent fall in production of thyroid hormone a sudden imbalance between the levels of thyroid hormone and follicular hormone in the blood led to the menorrhagia observed.

Josephine Barnes

493. **Ovarian Swelling and Intraperitoneal Bleeding as a result of Gonadotrophin Treatment.** (Svulne Ovarier med Blodning i Bughulen som Folge af Behandling med Gonadotropiner.)

By H. C. PETERSEN. *Ugeskr. Læg.*, **108**, 1351–1352, Nov. 28, 1946. 1 ref.

A nullipara, 21 years old, received two courses of treatment with gonadotrophins at 3-year intervals for hypo-oligomenorrhoea. Soon after the last course—15,000 units of "antex" and 4,500 units of "physex"—she developed acute abdominal pain with a palpable suprapubic tumour. At operation, a half-litre of blood was found in the abdomen; both ovaries were cystic and of a jelly-like consistency with infiltration of blood which had ruptured the capsule, one ovary being the size of a foetal head and the other the size of a fist. Resection of the former and suture of the latter were performed. Subsequent progress was uneventful.

494. **Mixed Synthetic Estrogens—Their Use in the Menopause.** (Dimethoxy Stilbestrol and Diethylstilbestrol.)

By O. H. BLOOM. *Amer. J. Obstet. Gynec.*, **53**, 263–265, Feb. 1947. 1 fig., 1 ref.

The disadvantages of treatment by repeated oral doses or by implantation of pellets of oestrogens are well appreciated. The author of this article has tried to overcome them by using a combination of stilboestrol and dimethoxystilboestrol in an oily solution. The dimethoxy product has to be demethylated to produce a response in the body and hence gives a prolonged action. There is an immediate response to stilboestrol which tides the patient over until the other product can act. Injections of 15 mg. of dimethoxystilboestrol and 1 mg. of stilboestrol in an oily solution are given weekly for three consecutive weeks. There appears to be genuine synergic action. The patient is free from symptoms [and treatment] for 4 months. In 56 patients observed, there were no toxic reactions; withdrawal bleeding occurred in 3 cases.

[This appears worthy of further trial.]

Kenneth Bowes

495. **Pathologic Findings in Genital Bleeding Two or More Years after Spontaneous Cessation of Menstruation.**

By D. B. CHEEK and J. E. DAVIS. *Amer. J. Obstet. Gynec.*, **52**, 756–764, Nov. 1946. 1 fig., 12 refs.

The results of a study of 514 cases of post-menopausal bleeding occurring in the Johns Hopkins Hospital over a period of 7½ years are recorded. No case was included in this study unless 2 years had elapsed since the last menstrual period. Patients referred for treatment for proved carcinoma were excluded. The complete investigation to which all cases, with few exceptions, were subjected included: (*a*) general physical examination, (*b*) gynaecological examination, (*c*) digital examination of anus and rectum, (*d*) urological survey, (*e*) haematological study, (*f*) biopsy of cervix, and (*g*) curettage of the uterus. The causes of the bleeding are tabulated below:

Pathological Findings According to Location.

Vulva:	
Carcinoma	2
Melanosarcoma of clitoris	1
Ulcer, non-specific (not granuloma)	2
Urethra:	
Carcinoma	5
Caruncle	10
Prolapse	2
Urethritis	1
Vagina:	
Carcinoma	1
Vaginitis, senile	60
Granuloma inguinale	1
Trauma	5
Pessary	5
Carried forward	95

	Brought forward	95
Cervix:		
Carcinoma		104
Polyp		37
Prolapse		35
Cervicitis, marked		36
Uterus Corpus:		
Carcinoma		58
Sarcoma of endometrium		2
Sarcoma in myoma		2
Myoma, submucous		18
Polyp, endometrial		18
Hyperplasia of endometrium		20
Endometritis, pyometra		6
Fallopian tube:		
Carcinoma		1
Tuberculosis		1
Ovary:		
Malignant		
Papillary cystadenocarcinoma 3; Medullary carcinoma 1; Krukenberg tumour 2; Granulosa-cell tumour 3		9
Benign		
Papillary serous cystadenoma 1; Serous cystadenoma 1; Pseudomucinous cystadenoma 2		4
Bleeding probably from oestrogen therapy		12
Unknown cause, including 7 cases with probable recrudescence of ovarian function		56
	Total	514

The authors emphasize the importance of a complete study of every case of post-menopausal bleeding irrespective of any obvious cause found on superficial examination. Out of the total of 514 cases 185, or 36.1 per cent were due to malignant growth and 329, 63.9 per cent to benign. When these figures are compared with those of similar surveys tabulated by the authors it is seen that the incidence of malignancy in the present series studied is considerably lower.

In analyzing their data the authors found that there was no significant racial difference in regard to aetiology, except that bleeding associated with prolapse of the cervix was uncommon in the negro race. The average age when the menopause was reached was 47.8 years, and when the age-groups are examined in relation to malignancy it is seen, as would be expected, that with increasing age there is a greater proportion of malignant lesions. The average duration of amenorrhoea for the entire series was 10.1 years. There was no correlation between the time the amenorrhoea had lasted and the cause of the bleeding, nor was the duration or type of bleeding in any way related to the causative lesion.

T. N. MacGregor

496. **Orientation in Gynecologic Uterine Bleeding.**
By C. E. McLennan. *Journal-Lancet*, **67**, 90–93, Mar. 1947. 5 refs.

497. **Postmenopausal Bleeding.**
By C. Macfarlane. *Penn. med. J.*, **50**, 598–601, Mar. 1947. 2 figs.

498. **Radium and Roentgen Therapy in the Treatment of Menopausal Uterine Bleeding.**
By H. E. Schmitz and J. E. Towne. *Amer. J. Obstet. Gynec*, **53**, 199–206, Feb. 1947. 1 fig., 8 refs.

Sterility.

499. **Sterility in the Female. Uterosalpingography and Resection of the Ovary.** (Esterilidad femenina. Uterosalpingografía y resección ovárica.)
By R. Peralta. *Med. Cirug.*, **11**, 101–116, Jan. 1947. 3 refs.

500. **Pregnancy following Hysterosalpingography with Unconfirmed Tubal Patency.** (Gravidanze successive ad isterosalpingografia con pervietà tubarica non accertata.)
By E. Robecchi. *Ginecologia*, **12**, 173–188, July-Aug. 1946. 45 refs.

The author considers that hysterosalpingography, in addition to its diagnostic value, has a therapeutic use in cases of sterility. Reports in the literature mention figures of up to 42 per cent of pregnancies after this procedure, in the majority of which the subject had previously been sterile. The author analyzes his feelings in 1,000 salpingographies. He has found that pregnancy subsequently occurs in 15 per cent of cases with normal tubal patency, 5 per cent of cases of unilateral tubal occlusion, 9.9 per cent of cases of impaired patency, and 9 per cent of cases of tubal occlusion. The author finds difficulty in explaining this fact. He considers that pregnancy may have followed the dilatation of the cervix or may have been aided by the active contraction of uterine and tubal muscle in response to the stimulus of the iodized oil. In addition, the

pressure of the oil may have freed the lumen from an obstacle. By increasing the pressure and maintaining oil within the tubes for a period of up to 2 hours he has often obtained filling of tubes previously regarded as occluded. Lipiodol (40 per cent) is introduced and maintained at a pressure of 200 ml. of mercury for 2 hours. In no case was any ill effect seen. Case reports are given of 5 patients who had an apparently complete obstruction and subsequently became pregnant, and of 5 other cases in which patency had been doubtful. The following factors which may lead to an incorrect diagnosis of sterility are mentioned. (1) It is recommended that the examination should be carried out at the time of maximal physiological permeability of the tubes. (2) A stenosis of the tubal lumen may be incorrectly interpreted as an occlusion. In such cases air insufflation may lead to the correct diagnosis. (3) Hypotonus of the uterine muscle may account for inadequate filling of healthy tubes. In such cases the atonic uterus appears to be pear-shaped and has a capacity of 6 to 8 ml. Contractions at the isthmus and the tubal angles are not seen and the emptying of the oil is prolonged. The use of drugs which provoke uterine contraction—for example, carbachol—is recommended. (4) Hypertonus is a more frequent finding, particularly in infantile and deformed uteri. Spasm may be responsible for the insufficient injection of the tubes. In these cases the giving of antispasmodics at least half an hour before the examination may help. (5) The oily solution, especially if of low concentration, may be quickly absorbed, so that the 24-hour film suggests an occluded tube. The above points are illustrated by case reports.

Hilde Eisner

501. **Tubal Sterility. Results of Operations.** (La stérilité tubaire. Résultats opératoires.)

By E. Douay. *Paris méd.*, **36**, 568–575, Dec. 21, 1946. 6 figs.

During the last 20 years the author has performed conservative operations on 64 sterile women, 27 on hospital patients and 37 in his private practice. The results in his hospital patients have been disappointing, no case of subsequent pregnancy having been recorded, but in his private practice 6 pregnancies leading to the birth of living children have followed (2 to the same woman) and one abortion. The disparity is possibly due to the poor follow-up in the hospital series, since pregnancy may occur long after a conservative operation for sterility. The preoperative examination must always include tubal insufflation and hysterosalpingography. At laparotomy, lesions may be much more extensive than investigation has indicated but hysterectomy should only be performed when absolutely necessary, since most patients prefer to cling to an even infinitesimal chance of becoming pregnant.

In the present series the operations are grouped as: (1) salpingostomy for adhesions at the fimbriated end of the tube; 10 operations, 4 pregnancies; (2) partial salpingectomy; 16 operations, no pregnancy; (3) tubo-uterine anastomosis; 2 cases, 1 pregnancy; (4) ovarian implantation into uterus; 6 cases, one abortion. The case histories of the successful operations are given in detail and the fact that emerges is the efficacy of early operation before permanent pathological changes have occurred in the mucosa and muscle of the Fallopian tube.

S. S. B. Gilder

502. **Surgical Treatment of Tubal Sterility.** (Treatmento cirúrgico da esterilidade tubária.)

By A. Campos da Paz Filho. *Rev. Ginec. Obstet.*, **40**, 286–294, Nov. 1946. 5 figs., 17 refs.

A successful salpingostomy for secondary sterility is described. The authors state that, in their opinion, the indications for this operation are very restricted (only 1 was performed out of a series of 296 cases of sterility investigated). The patient became sterile after an induced abortion 3 years earlier. She had a hydrosalpinx on the left side and an obstruction without dilatation at the fimbrial end of the right Fallopian tube. Salpingostomy with eversion of the tubal mucosa was performed at the abdominal ostia. Oestradiol benzoate, 1 mg. weekly, was injected post-operatively and prolonged short-wave therapy was also given. A hysterosalpingography showed that both Fallopian tubes were now patent. Eight months after operation, pregnancy which ended in abortion occurred, and a year later a normal pregnancy ended in the birth of a live child.

S. S. B. Gilder.

503. **Examination of Semen in Childless Marriages.** (Spermieundersokelse ved ufruktbare ekteskap.)

By M. Svendsen. *Tidsskr. Norske Laegeforen.* **67**, 11–13, Jan. 15, 1946. 1 ref.

After a brief mention of the history and the background of the subject, the author gives an account of the normal and abnormal findings in semen and their interpretation. It is estimated that about 10 per cent of marriages in Norway are childless and that probably this is a matter of choice in less than half.

Fresh ejaculate is described and attention drawn to the presence of blood (found in tuberculosis and tumours) and threads of mucus (found in prostatitis and vesiculitis). The volume comes mainly from the secretions of accessory glands and depends chiefly on the interval since the last ejaculation, but after 3 days should be at least 1.5 ml. Spermatozoa should be actively motile, but even in fertile men the proportion after half an hour may be as low as 40 per cent. Non-motile spermatozoa are assumed to be incapable of fertilization, but it must be remembered that motility is inhibited by hypotonic solutions, acidity (semen is weakly alkaline but the vaginal secretions are acid), and local disease. Semen without any motile spermatozoa is the cause of sterility in only 2 per cent of cases. The concentration of spermatozoa depends partly on the interval since the last ejaculation, but should be at least 60 million per ml. It is depressed with varicocele, in orchitis, and in a group of cases with soft testes and markedly abnormal heads in the spermatozoa. It is not altered in syphilis or gonorrhoea unless there is a stricture. Aspermia is found in testicular insufficiency and where there is obstruction to the channels of discharge. It is claimed by other authors to be the cause of 9 to 30 per cent of childless marriages; the author found it so in 14 per cent.

The morphology of the spermatozoa is very important, but up to 20 per cent of abnormal forms are found in fertile men. The commonest abnormality is a pyriform head, which is classed by some as an immature form and may occur in 20 per cent of the spermatozoa of fertile men. Another type is the round-headed spermatozoa. Hammen claims that areas of congenital hypoplasia can be demonstrated in almost every human testis, and suggests that round-headed forms are derived from these areas. A third type is the abortive form with undifferentiated head and lumps of cytoplasm or with a bent middle section. A fourth group contains the pathological forms—dwarfs, giants, those with many heads, and those with none. If the abnormal forms make up over 20 per cent they are usually either mainly round-headed and double forms, or mainly abortive and pyriform. The abnormalities are relatively constant for the individual and not affected by age. White blood cells may be found, often in association with a high percentage of pathological forms, but cultures are sterile.

The number and degree of abnormal findings indicate the likelihood of infertility: absolute sterility should be inferred only if repeated examinations show aspermia. Hammen found some abnormality affecting fertility in nearly all the wives, and abnormalities in the sperm of 53 of the husbands, in a series of 100 childless marriages. It is pointed out that the chance of having children is affected by the abnormalities on both sides, and that if the man has a poor ejaculate minor abnormalities, perhaps quite temporary, in the woman may be highly important and vice versa.

A. M. M. Wilson

504. **Contraception Masking Sterility and Infertility. Tubal and Seminal Factors in 1,000 Cases.**

By I. C. RUBIN. *J. Amer. med. Ass.*, **132**, 1047–1053, Dec. 28, 1946. 1 ref.

The author points out that the use of contraceptive methods is not infrequently resorted to by married couples who are actually sterile and in whom therefore contraception is unnecessary. Furthermore, as the couples do not know they are sterile treatment to cure sterility is not undertaken in the period soon after marriage, when it has a better chance of success than when delayed, as it often is, for a number of years. This applies both to cases of primary sterility where the patient has never conceived, and to cases of secondary sterility where contraception has been employed for varying lengths of time after one childbirth or after one or several spontaneous or induced abortions.

In the present paper the records of 1,000 cases of sterility have been analyzed to determine to what extent "reproductive stigmas" were present in the group of women who practised contraception as compared with those who did not. There were 711 cases of primary sterility and 289 of secondary sterility. In the former group, there were 466 couples who had used contraception during the first part of married life and 212 who had not. In 33 cases information was lacking.

In the examination of the records of the 466 couples who had practised contraception the major sterility factors were studied. This consisted in physical examination of wife and husband, utero-tubal insufflation, examination of semen, and determination of basal metabolic rate where indicated. The aetiological factors fell into 4 groups: (1) abnormalities of the pelvic organs; (2) endocrine dysfunction; (3) seminal inadequacy; and (4) tubal impairment. Bimanual examination with routine use of the vaginal speculum sufficed in most cases to determine the presence or absence of gross pelvic abnormalities. In a few, hysterography was used. The evaluation of endocrine dysfunction was limited to consideration of : (*a*) ovarian dysfunction as shown by amenorrhoea, hypomenorrhoea, oligomenorrhoea, menorrhagia, and metrorrhagia; and (*b*) hypothyroidism as demonstrated by a diminished basal metabolic rate.

In most cases Hubner's test was used for the study of semen, checked when necessary by examination of one or several samples brought in a glass container. The tubal status was determined by utero-tubal insufflation with carbon dioxide gas. Abnormalities of the pelvic organs or diseased conditions capable of diminishing fertility were found in 28.5 per cent. These included uterine hypoplasia, fibromyomata, retroversion, and cervical stenosis. As regards endocrine dysfunction, there were 19 women with menstrual difficulties and 15 with hypothyroidism, a total of 34 (7.3 per cent). Seminal inadequacy (azoospermia, necrospermia, or decided oligospermia) was judged to be present in 46.2 per cent. It is concluded that absence of spermatozoa by the Hubner test, even on several occasions, is not always conclusive evidence of male sterility, for normal spermatozoa may be demonstrable in the semen itself. Neither is absence of motility of the spermatozoa in the vaginal or cervical secretions 1 or 2 hours after coitus an absolute sign of infertility, for 47 out of 101 women in this series have become pregnant despite repeated evidence of non-motility.

Tubal status was determined in 353 of the 466 women; 51.6 per cent showed evidence of impairment. Of these, 21.3 per cent had non-patent tubes after several tests, 19.8 per cent had partially patent (from stricture or peritubal adhesions), and 10.5 per cent had spastic. To what extent the tubal impairment was present at marriage or acquired afterwards was not possible to determine.

Infertility factors were thus present in 80.3 per cent of the 466 women. This incidence might, however, be unduly high, as many of the cases had been of long standing or had proved refractory to all previous therapeutic measures—in short, they were a selected group. The seminal and tubal factors were the ones most often encountered, and this emphasizes the importance of a thorough examination of the semen and the tubal status. It should be noted that a prognosis cannot be given on any one specimen of semen. " At the present time one can only speak of the morphological characteristics, of estimated numbers of spermatozoa, and of the degree and type of motility. Actual insemination repeated over a certain length of time is necessary in order to determine its compatibility and ultimate fertility." In the group of 212 couples who did not use contraceptives the incidence of pelvic abnormalities, endocrine dysfunction, seminal inadequacy, and tubal impairment was substantially the same as in the first group.

The wisdom of determining the potential fertility of couples seeking contraceptive advice before such advice is tendered is discussed. The sooner the causal factor is determined and eliminated the better the prognosis; when the factor cannot be overcome it is better for the couple to know the facts as soon as possible. Unnecessary contraception may then be discontinued, psychological adjustment made, and, if desired, steps may be taken to adopt a child or for impregnation by a donor. In this series, however, it was estimated that only about 40 per cent had sought medical advice before practising contraception.

F. J. Browne

Abnormalities of the Reproductive Organs.

505. **Double Sclerosis of the Vagina.** (Eine Doppelsklerose der Vagina.)

By V. GRUENBERGER. *Wien. med. Wschr.*, **97**, 113–115, Mar. 8, 1947. 2 figs., 2 refs.

506. **A Case of Congenital Absence of the Vagina.**

By J. H. HANNAN. *Med. Press*, **217**, 270–271, Apr. 2, 1947.

507. **Bilateral Ovarian Aplasia.**

By C. A. ERSKINE and I. RANNIE. *Arch. Path., Chicago*, **42**, 381–390, Oct. 1946. 6 figs., 25 refs.

To the 6 undoubted cases of primary bilateral aplasia of the ovaries on record these authors add a seventh, which occurred in a white unmarried woman, aged 35 years, who died from pulmonary and abdominal tuberculosis. Clinically there was primary amenorrhoea with absence of secondary sexual characteristics. Necropsy showed that, although the genitalia were essentially female, they were not developed beyond the stage of prepuberty: there was complete absence of ovaries and no ectopic ovarian tissue was discovered. Histologically the tubes showed only evidence of recent tuberculosis. The epoophoron was carefully examined and resembled the normal in all essential aspects. One block contained a number of pigmented (iron-free) cells which were regarded as interstitial cells. The uterus, vagina, and breasts were all hypoplastic. The suprarenals were rather small and so was the thyroid, and its vesicles were filled with resting colloid. There was physiological involution of the thymus, but the pineal and pituitary glands showed no gross difference from normal.

The authors compare the findings in their case with those in the others recorded and summarize the main features in which they all agree. Variations do occur but are of minor importance, and the conclusion is reached that no specific changes in the other endocrine organs attributable to the absence of the ovaries can be found. Commenting upon the case, the authors discuss sex determination in relation to the primordial sex cells and their effect on the genital ridge. The influence of hormones on the further sexual development of the individual is also mentioned, and the opinion is formed that the usual genetic view of sex determination is actually supported by the occurrence of cases of bilateral ovarian aplasia.

R. B. T. Baldwin

See also No. 411.

Infections of the Reproductive Organs.

508. **Clinical Evaluation and Analysis of 268 Cases of Pelvic Infection.**

By I. TRACTENBERG. *J. int. Coll. Surg.*, **9**, 724–728 and 741, Nov.–Dec. 1946.

Some of the clinical features and the general lines of treatment adopted in the author's series of 268 cases of pelvic infection in women are discussed. The three main causes of pelvic infection are gonorrhoea, puerperal infection (pyogenic organisms, usually streptococci and staphylococci), and tuberculosis. Pyogenic infection is essentially a wound infection and spreads mainly by lymphatics, the characteristic lesion being a pelvic cellulitis; gonorrhoea is an infection to the mucous membrane of the genital tract and is an ascending infection to the mucosa of the tubes, whence it may spread through the other coats.

In this series infection was gonorrhoeal in 90 per cent of cases. Conservative treatment, including sulphathiazole, was used for all acute cases, and surgery was only indicated for drainage of an abscess. In subacute and chronic cases heat in the form of vaginal douches was used in addition to other measures. Posterior colpotomy was performed for residual pelvic abscesses; where abdominal operation was required both Fallopian tubes usually had to be removed, in which case a subtotal hysterectomy was done in addition. The mortality was 2.2 per cent.

[This article is written in too general terms to be of great value in assessing the merits of treatment].

L. W. Lauste

509. **Microbiology of Vaginal Flora.** (Mikronini obrazy posevní.)

By O. JIROVEC, R. PETER, and I. MALEK. *Ceskoslov. Gynaek.*, **12**, 1–24. 1947. 22 figs.

510. **Presence and Significance of the Anaerobic Vaginal Flora.** (Vyskyt a vyznam anaerobní posevní flory.)

By F. PATOCKA and V. SEBEK. *Ceskoslov. Gynaek.*, **12**, 24–36, 1947.

511. **A Study of the Bacterial Flora of the Normal and Pathologic Vagina and Uterus.**

By K. E. HITE and L. GOLDSTEIN. *Amer. J. Obstet. Gynec.*, **53**, 233–240, Feb. 1947. 32 refs.

512. **The Treatment of Mycotic Vulvovaginitis with Propionate Vaginal Jelly.**

By R. L. ALTER, C. P. JONES, and B. CARTER. *Amer. J. Obstet. Gynec.*, **53**, 241–244, Feb. 1947. 5 refs.

Mycotic vulvo-vaginitis is a common condition. A number of treatments have been tried with some degree of success, but all have the disadvantage that they are time-consuming for the patient and physician because applications have to be made two or three times weekly to the cervix, vagina,

and vulva. The treatment used by the writers, at Duke Hospital, Durham, N.C., has a high rate of cure and can be applied by the patient herself. The fungistatic substance employed is a propionate, in a jelly-like mixture, the formula of which is: Calcium propionate, 9.5 per cent; sodium propionate, 9.5 per cent; propionic acid, 1 per cent; glycerin, 10 per cent; "bentonite", 32 per cent; water, 38 per cent. The jelly is supplied in tubes with an applicator which holds 8 to 10 ml. The patient inserts the applicator, which is full of jelly, into the vagina, and deposits the contents in the upper vagina night and morning. Treatment is necessary for two or three weeks.

Gladys Dodds

513. **Hydrogen Ion Concentration (pH) of the Vagina Associated with an Ectropion of the Cervix (Cervicitis).**

By K. J. KARNAKY. *Amer. J. Surg.*, **73**, 359–362, Mar. 1947 2 refs.

514. **Syphilis of the Cervix.**

By W. F. GUERRIERO, W. B. MANTOOTH, and W. MOORE. *Sth. med. J.*, **40**, 261–264, Mar. 1947. 9 refs.

515. **The Present Status of Endocervicitis.**

By C. PANETTIERE. *Sth. med. J.*, **40**, 183–186, Feb. 1947.

This paper assesses the present status of endocervicitis and suggests a method for the treatment of this condition and of erosion of the cervix. The author states that 75 per cent of the adult female population is affected by this condition; his conclusions are based upon the observation of patients in South Florida, who come from all sections of the United States and the West Indies, representing a fair cross-section of the women of these countries. The lacerated cervix, malignancy of the cervix, and the postpartum cervix are not considered in his report. The outstanding manifestation of endocervicitis and erosion is a vaginal discharge, a symptom common to many diseases of the cervix and adnexa. The aetiological factors at work in the production of the condition are considered to include infection, hormonal influences, and abnormal anatomical positions of the uterus. In treatment the author employs a method which he considers the most satisfactory of the many he has used. The vaginal vault is thoroughly irrigated with a solution of warm mercury cyanide and the surface dried with gauze on a sponge holder. If the cervical canal is plugged with mucus—as is often the case—the plug is removed. The whole area is then sprayed with a 1 in 1,000 tincture of "merthiolate," followed by a generous spraying with "flumerin." Flumerin is a disodium salt of hydroxymercuri-fluorescein, containing 30 to 32 per cent of mercury in organic combination. Enough is left in the vault to saturate a small gauze tampon, and this is left for 24 hours in apposition to the cervix before removal by the patient. Local treatment of this nature is repeated twice weekly for an average duration of 3 weeks. At the end of that period the discharge has usually disappeared or has greatly diminished, and complete epithelization follows spontaneously. No contra-indication to the method, and no evidence of mercurial absorption, have been discovered.

Falkland L. Cary

516. **Torsion of Hydrosalpinx.** (Les hydrosalpinx tordus.)

By G. LEGRAND. *Brux. méd.*, **27**, 715–719, Mar. 30, 1947. 2 figs.

New Growths of the Reproductive Organs.

517. **Leucocytic Variations after Short-wave Applications in the Gynaecological Field.** (Variazioni leucocitarie dopo applicazione di onde corte nel campo ginecologico.)

By T. M. CAFFARATTO. *Ginecologia, Torino*, **12**, 237–248, Sept. 1946. 37 refs.

518. **Certain Pelvic Tumours Associated with Ascites and Hydrothorax.**

By M. CALMENSON, M. B. DOCKERTY, and J. J. BIANCO. *Surg. Gynec. Obstet.*, **84**, 181–191, Feb. 1947. 5 figs., 57 refs.

While the syndrome of ascites and hydrothorax associated with fibroma of the ovary has been described in medical literature from 1879, the syndrome was little known until the report by Meigs in 1937. The authors review the literature on this subject over a period of 60 to 65 years. They consider that the time has come (as Meigs and others anticipated) to include in the syndrome not only ovarian fibromata but also other benign and even malignant ovarian tumours. [They quote 2 published cases of recovery following removal of ovarian cystadenocarcinomata associated with

hydrothorax and ascites. The malignant nature of the tumour in itself was, therefore, not the cause of the ascites and hydrothorax.]

In the Mayo Clinic approximately 20,000 pelvic tumours were removed from 1910 to 1945. In 9 cases associated ascites and hydrothorax were also present. A tenth case was seen in 1946. The average age of these 9 was 48 years (extremes 36 and 67). Parity did not appear to be related to the development of the syndrome. Abdominal enlargement was the commonest complaint. The tumours found were 4 ovarian fibromata, 1 ovarian fibromyoma, 1 degenerating uterine fibromyoma, 1 fibromyoma of uterus with pelvic inflammatory adnexal disease, 1 granulosa-cell tumour of the ovary and 1 complex teratoma of the ovary. The tenth was a cystic fibroma of the ovary. The end-results of surgical treatment in all 9 cases (the result in the tenth is not discussed) were excellent. Neither ascites nor hydrothorax recurred. (The longest follow-up was 27 years.) Theories of the aetiology of the ascites and hydrothorax in this syndrome are discussed *in extenso*.

Anthony W. Purdie

519. **Prevention of Female Genital Cancer.** (Prevençao do câncer genital femino.)

By A. H. Rocha. *An. brasil. Ginecol.*, **22**, 467–473, Dec. 1946. 4 refs.

520. **Carcinoma of the Vulva. Results of Treatment and Effect of Special Factors on Results.**

By F. R. Smith and R. S. Pollack. *Surg. Gynec. Obstet.*, **84**, 78–84, Jan. 1947. 1 fig., 21 refs.

The authors discuss a series of cases of carcinoma of the vulva treated in the Memorial Hospital, New York, from 1926 to 1945. Of 244 cases, 167 were primary and 77 cases had received previous treatment. Of the primary cases 100 have been observed for a period of 5 years or more and evaluation of the results of treatment is based on these. Although carcinoma of the vulva accounts for only 4 per cent of all cases of malignancy in the genital tract, it is important because it provides an opportunity for early diagnosis and even prevention; the poor results, however, indicate a failure to take adequate advantage of these facts. The growth is essentially a skin carcinoma, but presents special features owing to the anatomy and rich lymphatic drainage of the vulva.

In this series the youngest patient was 27 years old, and the oldest 89 years, the main incidence occurring in the 60 to 69 age-group; 86 per cent were married or widows, and 14 per cent single; 75 per cent had one or more children, and 25 per cent were nulliparous. Eight of the patients had syphilis and 10 diabetes, but these conditions did not appear to be of significance. Pruritus, pain, and bleeding were the common symptoms, and 70 per cent of the patients presented themselves because of the lesion. The authors stress the importance of pruritus as a symptom which occurs in over 50 per cent of patients, and state that 36 per cent of the patients had leucoplakia. Histologically, 89 cases were of epidermoid carcinoma, 25 of melanoma, 9 of basal-celled carcinoma, 1 of adenocarcinoma of Bartholin's gland, 1 of vulvar Paget's disease, and 1 of dermatofibrosarcoma protuberans. Thus 84 per cent were epidermoid carcinomata and two-thirds of these were grade II carcinoma. The percentage of melanoma was unduly high.

In the period 1926–40 there were 100 cases of primary carcinoma and 46 cases previously treated. The absolute 5-year cure rate in both groups was 26 per cent. The cases were also analyzed in various sub-groups to determine the influence of different factors on end-results. These groups were: (1) Cases with involvement of the lymph nodes: A, clinically; B, histologically. (2) Cases with involvement of the lymph nodes and operable; A, clinically; B, histologically. (3) Inoperable cases. Graphs of the survival rates of these groups showed the highest rate to be in Group 1 B (80 per cent) with a marked fall in Group 2 (about 10 per cent of 5-year survivals) and no 5-year survivals in Group 3.

All cases were treated by surgery, X-rays, or radium, or by a combination of these methods. Surgical treatment included simple vulvectomy, vulvectomy with excision of the nodes on one or both sides, and vulvectomy with a Bassett type of node dissection. The results show that the prognosis is much worse if the lymph nodes are involved, and indicate the advisability of removing them. The results in cases treated with X-rays alone or by vulvectomy with X-rays or radium were less good than those obtained by surgery. It was possible in most cases to determine the site

of origin of the growth, and it appeared that the prognosis was least good in growths of the clitoris; 59.6 per cent occurred in the labia majora, 21 per cent in the labia minora, 27 per cent in the clitoris, and 3.8 per cent in the region of the posterior commissure. The prognosis was worst with melanoma and best with basal-celled carcinoma and epidermoid carcinoma of Grade I. The cases previously treated were analyzed separately, and the general findings were in keeping with those of the primary group, the absolute 5-year survival rate being exactly the same—namely, 26 per cent.

It is concluded that in all cases suitable for surgery, vulvectomy with dissection of the lymph nodes should be done. It was not possible to say whether the Bassett type of dissection had any advantage nor, from the figures, could it be judged whether a one-stage or multiple-stage operation was best. In view of the malignancy of melanoma it was considered advisable to remove all pigmented tumours.

L. W. Lauste

521. **Fibroadenoma of Supernumerary Mammary Gland Tissue in Vulva.**

By J. H. FISHER. *Amer. J. Obstet. Gynec.*, **53**, 335–337, Feb. 1947. 2 figs., 7 refs.

522. **A Case of Bowen's Disease of the Vagina.** (A propos d'un cas de maladie de Bowen vaginale.)

By J. FIGARELLA. *Rev. franç. Gynéc.*, **41**, 347–351, Nov. 1946.

Bowen's disease of mucous membranes occurs in women aged 40 to 73; it is slowly progressive, lasting on the average 11 years; the aetiology is unknown, but it occasionally follows kraurosis vulvae; it may be situated anywhere in the mucosa of the genital tract. The earliest lesion is a small papule, which gradually increases in size and multiplies. Many consider it to be a precancerous condition. It must be distinguished from syphilitic, tuberculous, and diabetic lesions, but the only condition which is very difficult to differentiate from Bowen's disease is the "erythroplasia of Queyrat" or "denuded papillary epithelioma of Darier"; in fact, this last dermatosis and Bowen's disease may be two different aspects of the same condition. Bowen's disease of mucous membranes was first described in 1921 by Jessner, who published 2 cases. Since then several cases have been published. Of all cases of Bowen's epitheliomatous dyskeratosis, about 22 per cent are situated in mucous membranes. The author describes a case in a 61-year-old patient, who complained in 1942 of blood-stained vaginal discharge for 4 months, with no pain but with lower abdominal discomfort. The menstrual history was normal; 10 pregnancies had resulted in 5 miscarriages and 5 deliveries. The perineum and vulva were healthy, the uterus and adnexa normal. The vaginal wall was covered by small granular elevations, quite smooth, red in colour, and there was a serous blood-stained exudate. Biopsy demonstrated very hypertrophied epithelium, undifferentiated Malpighian cells—many of which showed mitosis, some atypical and some with giant nuclei; the submucous layer was normal. The lesions were cauterized and apparently healed, but have gradually returned and now, 3 years later, are just as abundant without exhibiting any malignant change.

Nicolas Tereshchenko

523. **Modern Trends in the Management of Uterine Carcinoma.**

By F. L. PAYNE and G. L. HOFFMAN. *Penn. med. J.*, **50**, 491–496, Feb. 1947. 38 refs.

524. **The Vaginal Smear. Practical Applications in the Diagnosis of Cancer of the Uterus.**

By J. V. MEIGS. *J. Amer. med. Ass.*, **133**, 75–78, Jan. 11, 1947. 6 refs.

The use of smears from the vagina in the diagnosis of uterine cancer is reviewed by the author, who has experience of 2,749 examinations in the Massachusetts General Hospital, in which series the method gave an error of only 3.2 per cent.

Detailed technique is given by Papanicolaou and Traut (*Amer. J. Obstet. Gynec.*, 1941, **42**, 193). Briefly the method consists in aspirating vaginal secretion into a glass tube with a rubber suction bulb and blowing the secretion on to a glass slide, then spreading the secretion into a thin film and fixing immediately in equal parts of ether and 95 per cent alcohol. The film is subsequently stained. Diagnosis depends on recognition of abnormal nuclear pattern in shed cells and demands of the pathologist considerable experience of the technique, besides being a time-consuming procedure. Additional help may be obtained from the presence of leucocytes and red cells in the smear. This method is preferred to more elaborate ones which

use endocervical catheters, as its simplicity brings it within the range of the general practitioner. Moreover, the vaginal secretion contains cells derived from the entire uterine mucosa and so may be more accurate.

The diagnosis by smear of cancer of the cervix is simple, as cancer cells are unmistakable. False positive results (amounting to 2 per cent of the author's series) are probably explained by early growths being missed in serial sections after hysterectomy. False negative results were obtained in 3·5 per cent of cases of cervical cancer, and are to be explained either by the growth not shedding cells or by preliminary douching by the patient. In endometrial cancer confusion between malignant and non-malignant cells in smears is not infrequent, and more expert observation is thus demanded. False negatives were obtained in 20 per cent of the author's series of 80 endometrial cancers.

The author regards this method as of proved value in making an early diagnosis of uterine cancer. Of his series of 339 cases of this condition, in 25 cases early diagnosis depended upon or was materially assisted by vaginal smears. It is particularly valuable in following up cases of cancer previously treated by irradiation, although diagnosis in such cases is more difficult than usual. It is emphasized that this method can be more accurate than biopsy, but radical surgery on the strength of positive smears only is not advised at present. Some illustrative cases are recorded.

T. N. MacGregor

525. **A Review of the Vaginal Smear Method for Early Diagnosis of Cancer. (Report of Cases.)**

By G. W. McCLURE. *W. Virginia med. J.*, **43**, 66–71, Feb. 1947. 8 refs.

526. **Uterine Chorionepithelioma with Severe Intraperitoneal Haemorrhage.**

By C. V. SALISBURY, and B. C. GLASGOW. *Med. J. Austral.*, **1**, 334-336, Mar. 15, 1947. 1 fig., 10 refs.

527. **Corpus Carcinoma. A Study of Three Hundred and Twenty-two Cases.**

By N. F. MILLER and C. W. HENDERSON. *Amer. J. Obstet. Gynec*, **52**, 894–903, Dec. 1946. 9 refs.

The authors, impressed by the comparatively poor long-term results following total hysterectomy with removal of Fallopian tubes and ovaries in carcinoma of the corpus uteri, have, for the past 14 years, been using a combination of pre-operative irradiation either by X-rays or radium, followed by panhysterectomy 6 weeks later. They now favour pre-operative X-ray irradiation, and the results achieved by this combination in 96 cases were as follows: 84.7 per cent of patients survived for 3 years; 77 per cent for 5 years; and 65 per cent for 10 years. The uterus, Fallopian tubes, and ovaries are carefully examined histologically after removal; 15 specimens (15.6 per cent) revealed no carcinoma. From this extensive experience the authors have formed the following impressions: (1) pre-operative X-ray irradiation has proved to be a valuable adjuvant to total hysterectomy and bilateral salpingo-oöphorectomy in the treatment of carcinoma of the corpus uteri; (2) its use clears the uterine infection, reduces uterine size, and decreases pelvic hyperaemia, thereby facilitating operation; (3) pre-operative X-ray irradiation has not in any discernible way interfered with wound healing.

F. J. Browne

528. **Radiation Therapy of Uterine Myoma. Critical Analysis of Results in Five Hundred Cases, showing Indications and Limitations.**

By R. J. CROSSEN and H. S. CROSSEN. *J. Amer. med. Ass.*, **133**, 593–599, Mar. 1, 1947. 3 refs.

A review is made of 549 cases of uterine myoma treated, 90 per cent successfully, during the last 20 years. The authors recommend radiation therapy for certain selected cases of myoma, with undue bleeding in older women. Of the patients, 7 per cent were under 40, 61 per cent between 40 and 50, 30 per cent between 50 and 60, and 2 per cent over 60 years old. The suitable case for irradiation is one where the uterus is the size of a fist or smaller (456 cases in this series with 31 failures). Irradiation was given to 53 tumours of grape-fruit size, with 5 failures, and to 17 cases where the uterus was enlarged almost to the umbilicus, with no failures. Supplementary irradiation was given to 23 of the failures with successful results. The length of time required for success was 6 months in 50 per cent of the cases.

The authors state that when pelvic pain or pressure discomfort is a prominent feature there is little likelihood of a satisfactory result. They believe that there are four necessary steps for the safe handling of the case by radiation therapy: (1) deep pelvic palpation under anaesthesia to exclude ovarian or adnexal disease; (2) curettage to exclude

carcinoma of the uterus; (3) conization of the cervix to remove a source of chronic irritation and possibly to prevent the development later of carcinoma of this area; and (4) accurate recordings of findings at the time of examination.

At the primary examination 23 of the 549 cases were found to have carcinoma of the uterus as well, and a further case had an early carcinoma of the cervix missed at the first examination; 526 cases were therefore treated by the usual radiation dosage (1,200 to 2,400 mg.-hours) to stop myomatous activity and induce an artificial menopause. There were 30 failures. In 6 cases degeneration of the myoma occurred, necessitating operative treatment; in 4 the bleeding continued, as the fibroid was submucous, and hysterectomy was performed; in another 4 cases continuation of bleeding was associated with carcinoma of the endometrium; in 1 there was endometrioma of the uterus; in 2, endometriosis of the adnexa; in 2 carcinoma of the ovary; in 1, simple cyst of the ovary; and in 5 cases chronic salpingitis. Three patients subsequently developed stenosis and pyometra.

The authors claim that 90 per cent success with radiation therapy in 470 patients was obtained with minor risks. The alternative method of treatment would have entailed a major abdominal operation. They further point out the advantage of this treatment in that the patient submits herself at an earlier stage of the disease when she might be inclined to postpone a major surgical operation.

Gladys Dodds

529. **The Place of Myomectomy in the Treatment of Myoma Uteri.**

By M. S. QURESHI. *J. Obstet. Gynaec., Lahore,* **7**, 169–178 and 183–190, Nov. and Dec. 1946. 28 refs.

530. **Surgery in the Uterine Fibroid, a Plea for Myomectomy.**

By J. W. ROSS. *Amer. J. Obstet. Gynec.,* **53**, 266–270, Feb. 1947.

531. **Carcinoma of the Cervix.**

By W. P. SMITH. *Med. Times, N. Y.,* **74**, 32–35, Jan. 1947.

532. **Clinico-statistical Notes on Cancer of the Cervix Uteri.** (Note clinicostatistiche sul cancro del collo dell' utero.)

By L. CUSMANO. *Ginecologia, Torino,* **12**, 249–284, Sept. 1946. 37 refs.

533. **Carcinoma of the Cervix During the First Two Decades of Life.**

By R. S. POLLACK and H. C. TAYLOR. *Amer. J. Obstet. Gynec.,* **53**, 135–141, Jan. 1947. 1 fig., 25 refs.

534. **The Effect of Radiation on Vaginal Cells in Cervical Carcinoma. I. Description of Cellular Changes.**

By R. M. GRAHAM. *Surg. Gynec. Obstet.,* **84**, 153–165, Feb. 1947. 22 figs., 9 refs.

This study comes from the Vincent Memorial Laboratory of the Massachusetts General Hospital, Boston. Vaginal-smear studies were made in 206 cases of cervical carcinoma (27 adenocarcinomata and 179 epidermoid carcinomata) treated by X-rays, radium, or both.

The author first describes the normal vaginal-cell picture and illustrates basal, precornified, and cornified cells and histiocytes. Differentiation or non-differentiation of the malignant cells of epidermoid carcinoma depends on how advanced the tumour is. In adenocarcinoma they are undifferentiated. The cases are divided into four groups: (1) those studied during their radiotherapy; (2) those with a follow-up beginning from 1 to 6 months after treatment; (3) those whose follow-up began at 6 months to 1 year after treatment; and (4) those whose treatment took place 1 to 15 years before the first vaginal smear was taken.

The first group, the 35 cases of cervical carcinoma, fall into 2 classes: (1) those showing definite irradiation in all cells, and (2) those showing very little effect in either normal or malignant cells. The first effect of irradiation is seen in normal cells. The basal cells, by the ninth or tenth day of treatment, lose their round appearance and become elongated while retaining a normal vesicular nucleus: many change their staining reaction from a basophilic to a brownish colour by Papanicolaou's method. Later the nuclei become degenerate. About the twelfth day the cells become greatly increased in size, but the cytoplasmic-nuclear ratio remains constant. About the fifteenth day progressive cytoplasmic vacuolization occurs. Finally the cells become very bizarre in shape. The precornified cells enlarge two to three times in size (fifteenth day), the cytoplasmic-nuclear ratio remaining constant. Their nuclei acquire a dead pyknotic appearance and may become fragmented. The cytoplasm becomes

vacuolated and bizarre, and polymorphonuclear leucocytes become included later in the cells themselves. Similar changes, other than the nuclear ones, occur in the cornified cells. In malignant cells, post-irradiation changes begin usually by the eleventh day. The cells increase in size, their cytoplasm become vacuolated, and they frequently contain several nuclei which appear dead. It is often difficult to say whether an irradiated cell was originally malignant or benign. Nearly half of the cases in this group showed an increase of malignant cells after irradiation had begun. On an average, however, malignant cells have disappeared by the twenty-fourth day after irradiation has begun. Five cases whose treatment was adequate showed little reaction either in malignant or in normal cells.

In the second group, consisting of 50 cases, 18 showed irradiation changes similar to those described above, while 32 did not. In the third group, of 19 cases, 11 showed the expected irradiation reaction, 4 had none, and 4 showed evidence of post-irradiation recurrence of the growth.

The fourth group consisted of 102 cases. If divided by the type of cell found in the smear they fall into three categories. Approximately one-third show only basal cells, one-third precornified cells and basal cells, and the remainder cornified, precornified, and an occasional basal cell. This is not an age difference. Eight showed signs of recurrence.

The author points out that the changes seen in individual cells, both normal and malignant, are comparable to those previously described by workers who have studied biopsy specimens from irradiated patients. Vaginal smear is easier to perform than a biopsy, and can be done much more frequently. Although it does not indicate the depths of the neoplasm, the vaginal smear does show representatives of the entire cell population of the vagina and cervix. Its possible prognostic significance is discussed in a succeeding paper.

Anthony W. Purdie

535. **Endometriosis: Diagnosis and Treatment.**
By J. RYAN. *Med. Press*, **217**, 215–218, Mar. 19, 1947.

536. **Endometriosis and Adenomyosis.**
By Y. C. YIN. *West. J. Surg.*, **54**, 490–493, Dec. 1946. 7 refs.

The terms endometriosis and adenomyosis have often been used synonymously. The author prefers the term adenomyosis for intrauterine aberrant proliferation and endometriosis for extrauterine endometrial conditions. Both are common in Chinese women, most of the patients coming from the upper social class. Endometriosis was commonest between 19 and 32 years, and adenomyosis between 30 and 45 years. Cases of endometriosis outnumbered those of adenomyosis by three to one.

None of the theories so far advanced for the pathogenesis of endometriosis explains all its clinical and pathological manifestations. The conception is gaining ground that excessive ovarian secretion may activate, if not cause, excessive endometrial proliferation. A case is quoted in support of the implantation theory, though it is not claimed that this explains all cases of pelvic and abdominal endometriosis. For adenomyosis it seems likely that a congenital origin, in fact a maldevelopment of the Müllerian ducts, is responsible. Two cases illustrating this are quoted. On the other hand, cases are quoted where, on account of congenital atresia of the vagina, the pelvis was full of tarry, dammed-up blood without any evidence of endometriosis. This is given in support of the idea that excess ovarian secretion is responsible for the activation and maintenance of ectopic endometrial tissue.

The symptoms are briefly described. The belief that adenomyoma is commonly found in retroverted uteri is not substantiated by clinical experience, nor is sterility a diagnostic point.

[The chief interest in this paper, which otherwise contains little that is original, lies in the statement that endometriosis occurs in Chinese women at such an early age. This may be owing to the earlier occurrence of puberty.] *Josephine Barnes*

537. **Some Cases of Ovarian Malignancy.**
By J. S. QUIN. *Irish. J. med. Sci.*, 121–125, Mar. 1947.

538. **Cornification in Ovarian Carcinoma.** (Uber Hornbildung in den Ovarialkarzinomen.)
By R. KLEITSMAN. *Acta. obstet. gynec. scand.*, **27**, 46–57, 1947. 3 figs., 14 refs.

539. **A Case of Sarcoma of the Ovary and of Developmental Anomaly in a 13-year-old Child.** (Sopra un caso di sarcoma dell'-ovaio e di anomalia di sviluppo genitale in una bambina di 13 anni.)
By L. U. BARBERIS and U. FONTANA. *Minerva med., Torino*, **38i**, 310-313, Mar. 24, 1947. 3 figs.

540. **Meigs's Syndrome in Theca-cell Tumor of the Ovary.**

By L. E. FRANKENTHAL. *Amer. J. Obstet. Gynec.*, **53**, 331, Feb. 1947.

541. **Tubular Adenomas and Testis-like Tubules of the Ovaries of Aged Rats.**

By E. T. ENGLE. *Cancer Res.*, **6**, 578–582, Oct. 1946. 5 figs., 4 refs.

A histological examination of the ovaries of aged Wistar rats revealed that a proportion of these ovaries contained tubular adenomata with characteristic epithelial cells showing vague cytoplasmic borders and grooved nuclei closely resembling the Sertoli cells of the seminiferous tubules of rat testis. This type of nucleus has also been found in the Brenner tumour and occasionally in connective tissue, smooth muscle, and ordinary epithelium. Other workers, using the ovaries of a shrew, have demonstrated that the ageing factor in the animal is not dominant. The authors conclude: " The thoughtful suggestion of Robert Meyer that the arrhenoblastomas and other dysgerminomas probably arise from persisting embryonic influences may also apply in these cases of testis-like tubules in the ovaries of aged rats. In these cases, however, the restriction of the tubules to rats in the oldest age groups possibly indicates a type of android proliferation which was permitted only after removal of gynecoid influences."

I. Hieger

542. **Pathology and Physiology of Struma Ovarii.**

By F. G. SMITH. *Arch. Surg., Chicago*, **53**, 603–626, Dec. 1946. 6 figs., 137 refs.

Ovarian dermoids are often found to contain thyroid tissue if examined in sufficient detail, but the term " struma ovarii " should be confined to ovarian tumours in which thyroid tissue is a major constituent. Such tumours are uncommon. The author tabulates, with brief particulars, the 152 cases recorded in the literature and includes a case of his own. About one-half are examples of dermoids containing, besides thyroid as a major constituent, such tissues as skin, teeth, brain, and intestinal epithelium. One-third are ovarian cystomata, either serous or pseudo-mucinous, containing thyroid. The remaining one-sixth are pure thyroid tumours of the ovary. The author's case belongs to the last and rarest group.

A woman of 58, known for 2½ years to have had a small nodular goitre with mild hyperthyroidism, complained of pelvic discomfort and frequency of micturition. On examination the right lobe of the thyroid was found to contain a firm nodule 2 cm. in diameter, and a round hard mass was felt in the left adnexa. Operation revealed a solid tumour of the left ovary 5 cm. in diameter, the pelvic viscera being otherwise normal. Bilateral salpingo-oöphorectomy was done. Pathological examination of the tumour showed it to be composed of remnants of ovary, normal thyroid tissue, thyroid adenoma, and small foci of osseous formation. The thyroid adenomatous tissue was distributed throughout the tumour in nodules. In places there was evidence of a malignant tendency, the cells showing very active proliferation and invading blood vessels. The patient was alive and well 6 years later.

Close study of the reported cases has brought out the following points. Ovarian strumata occur at all ages, though they are exceedingly rare before 25. An associated cervical goitre is not uncommonly present. Metastases, which may be highly malignant, occur occasionally, local peritoneal implants, and spread to the liver and the bones having all been recorded. Microscopically the appearance of malignancy is often seen. However, it is pointed out that the histological criteria of thyroid malignancy are difficult to formulate, and that it is sometimes held that invasion of the blood vessels is the only reliable distinction between benign and malignant adenomata. The author's case showed this invasion, but metastasis had not occurred. The significance of foci of calcification and ossification, which have often been noted and were present in the author's case, is discussed. The conclusion is reached that they are similar to the calcification and ossification frequently seen in cervical goitres and that their presence is not itself evidence of a teratomatous tumour process. Notwithstanding this the author is of opinion that all ovarian strumata are in fact of teratomatous origin. About 10 per cent of the cases have had thyrotoxic symptoms, and removal of the ovarian struma has led to improvement in a few. This did not occur in the author's patient, whose basal metabolic rate, known to be +19 per cent 2½ years before the operation, remained at about this level afterwards, no doubt because of the coexistent nodular goitre.

[This is a clear and very comprehensive study of

a small subject. There is a complete bibliography. The photomicrographs are of exceptional quality.]

H. J. Croot

543. Solid Teratomas of the Ovary with Neurological Metastases.

By G. G. PROSKAUER. *Amer. J. Obstet, Gynec.*, 52, 845–849, Nov. 1946. 3 figs., 20 refs.

Only 10 cases of peritoneal implantation of nervous tissue derived from an ovarian teratoma have been reported. The rarity of the condition is the reason for reporting this additional case of neuroglial metastasizing ovarian teratoma. The patient, aged 22, had a 4-months history of abdominal pain and swelling. Colostrum was present in both breasts, the Aschheim-Zondek reaction was negative, and there was considerable ascites. Two ovarian tumours were found; that on the left side was a simple dermoid cyst; but the tumour of the right ovary, a good deal larger, was shown to be a teratoma, of which about one-sixth consisted of fat tissue and the remainder mainly of nervous tissue, with here and there islands of hyaline cartilage, mucous glands, sebaceous glands, and hairs. The greater part of the tumour was composed of neuroglia, in some regions having gyrus-like structure. Here and there ganglion cells were found, mature in appearance and with nuclei, nucleoli, axons, and dendrites. No myelin sheaths were seen. In the upper pole of the tumour a completely developed cerebellar cortex was found, having the normal appearance of an internal granular layer, a single layer of Purkinje cells, and an external grey substance. Secondary (implantation) growths were scattered through the greater omentum, which was adherent to the right ovary. These nodules contained neuroglia but neither ganglion cells nor neuro-epithelium. Fifteen months after post-operative X-ray treatment the patient was in good condition.

T. C. Clare

544. Brenner Tumours of the Ovary. (Ueber die Brenners'chen Ovarialtumoren.)

By R. KLEITSMAN. *Acta obstet. gynec. scand.*, 27, 33–45, 1947. 2 figs., 28 refs.

545. Masculinizing Tumours of the Ovary. A Clinicopathologic Survey with Discussion of Histogenesis and Report of Three Cases.

By L. IVERSON. *Surg. Gynec. Obstet.*, 84, 213–238, Feb. 1947. 15 figs., 126 refs.

Much of the previous literature on the subject of virilizing tumours of the ovary is reviewed. Though individual workers differ in their classification of these tumours the consensus is that there are two main types—the arrhenoblastoma and the less common virilizing lipoid-cell tumour. The latter has been given various names, most of which suggest a connection with the adrenal cortex, such as hypernephroma of the ovary and ovarian adrenal rest. The author compares the published data concerning 41 cases recorded as arrhenoblastoma and 24 examples of virilizing lipoid-cell tumour, mostly reported as adrenal tumours of the ovary. The average age of patients (32 years), age distribution (from 15 to over 60), and average duration of symptoms before operation (4 years) were the same in both groups. Amenorrhoea was always present. Virilism, as shown by hirsutism, voice change, breast atrophy, and hypertrophy of the clitoris (not all necessarily in every patient) was invariably found in the cases of virilizing lipoid-cell tumour and in all those of arrhenoblastoma except the most highly differentiated type, usually known as testicular adenoma of the ovary. The only pure examples of this type, 6 in number, showed no virilizing symptoms. Hypertension and diabetic tendencies were found occasionally in both groups; there was nothing to support the view sometimes expressed that they are especially characteristic of the lipoid-cell tumours. The incidence of malignancy was equal, about 10 per cent in both groups. In assessment of prognosis as regards malignancy no help was gained from the histological appearance of the tumour, the least differentiated and most sarcomatous-looking arrhenoblastoma often proving clinically innocent. A rapidly growing tumour, ascites, loss of weight, and return of symptoms after operation were the usual indications of malignancy. The lipoid-cell tumours were smaller and had less tendency to cyst formation. When cut across they showed a characteristic yellowish-orange colour due to intracellular lipoids.

Detailed histological studies were made in the Department of Pathology, Duke University, Durham, N.C., of the tumours from 4 cases, including the 3 here reported. Although the resemblance of the lipoid-cell tumour to adrenal tissue is very striking the author puts forward the view that both types of virilizing tumour are in fact of

true ovarian origin, having a common ancestry from the theca lutein cells. Strong support for this point of view is afforded by one of the author's cases. A large ovarian tumour was removed from a woman of 61 with signs of virilism. The greater part of the tumour was typical of arrhenoblastoma, but a large nodule was present composed of adrenal-like tissue. Further, the only metastasis, a peritoneal implant, contained cells characteristic of both types of tumour.

H. J. Croot

546. **Masculinizing Tumor of the Ovary of the Adrenal Type.**

By M. DOUGLASS. *Amer. J. Obstet. Gynec.*, **53**, 190–198, Feb. 1947. 10 figs., 10 refs.

547. **Torsion of a Seminoma of the Ovary.** (Séminome tordu de l'ovaire. Intervention d'urgence.)

By M. FATIO. *Mém. Acad. Chir., Paris*, **73**, 23–24, Jan. 15 and 22, 1947.

A 48-year-old nullipara was admitted to hospital with a history of vague abdominal and pelvic pain and dysuria. For 3 years she had only menstruated 2 or 3 times a year. Catheterization revealed the presence of 600 ml. of residual urine, and subsequent examination disclosed a large, almost fixed mass to the right of the uterus. Two days later, the patient had a sudden onset of hypogastric pain, and vomited. Palpation of the right iliac fossa and of the right fornix was painful. Immediate laparotomy was performed, and a cyst of the right ovary (of the size of a foetal head) was found to have undergone torsion of its pedicle through 360 degrees. Puncture gave a haemorrhagic liquid. Salpingo-oöphorectomy was performed. Macroscopically, the cyst showed haemorrhagic areas in its wall and an intracystic papilloma of the size of a tangerine. Microscopically, areas with typical structure of a seminoma were found. Estimation of the daily prolan-A excretion in the urine gave a value of 420 rat units. Since it was thought probable that metastases in the lymph nodes were responsible for this finding, X-ray irradiation of the lumbar region was carried out, after which urinary examination for prolan-A became negative.

S. S. B. Gilder

548. **Clinical and Pathologic Aspects of Primary Sarcoma of the Uterine Tube.**

By L. C. SCHEFFEY, W. R. LANG, and F. B. NUGENT. *Amer. J. Obstet. Gynec.*, **52**, 905–916, Dec. 1946. 3 figs., 44 refs.

Primary sarcoma of the Fallopian tube is rare and during the last 60 years only 21 cases have been reported. In the same period 578 tubal caricinomata have been reported, a ratio to tubal sarcoma of about 25 to 1. The authors describe a case of their own. The patient, aged 70, had had 1 pregnancy and was admitted complaining of low pelvic pain with intermittent vaginal discharge, sometimes bloody. The menopause occurred at the age of 55, and 10 months before admission there had been a sudden, rather profuse haemorrhage, for which a diagnostic curettage was done and an intrauterine application was made of radium (1,200 mg. hours). The report on the curettage showed an atrophic endometrium but no malignancy. After this treatment an intermittent bloody vaginal discharge was noted. Nine months later, pelvic examination revealed an extremely tender, enlarged, retroflexed uterus with no apparent abnormality in the appendages. A diagnosis of pyometra was made. Vaginal smear (Papanicolaou technique) showed atypical cells suggestive of fundal carcinoma. Laparotomy exposed an atrophic uterus displaced forwards by a more or less fixed swelling in the cul-de-sac, apparently a left pyosalpinx adherent to the uterus. There was no evidence of peritoneal implants and the regional glands were not enlarged. The diagnosis at operation was a left pyosalpinx resulting from radium application. Complete hysterectomy with bilateral salpingo-oöphorectomy was carried out. Recovery was uneventful.

Examination of the removed structures showed that the middle and outer thirds to the left Fallopian tube weer replaced by a grey friable tissue. The fimbrial end was sealed. The inner third of the tube was distended with blood and the wall was very thin. Microscopically the growth was composed of a "very cellular and bizarre growth made up of muscle cells and some fibroblasts"—a myosarcoma of the mixed-cell variety. At the time of writing, 2 years after operation, there is no evidence of recurrence.

The authors discuss the clinical features of the reported cases. The age incidence ranged from 27 to 70. In pre-menopausal patients, menorrhagia or metrorrhagia usually occurred and often, also, an abnormal vaginal discharge, either serosanguineous or semipurulent. In the post-menopausal

groups the discharge was generally bloody but sometimes profuse and watery. In 2 young patients, aged 27 and 37, the menses were normal. In nearly every case pain was a prominent symptom. In no case was the diagnosis made preoperatively. In 6 cases the tumour was bilateral. The authors emphasize the similarity of the clinical features to those of tubal carcinoma. Vaginal bleeding is not so well marked as in uterine cancer but is more often a watery, blood-stained discharge. Pain is the most constant and conspicuous symptom and is often associated with gastro-intestinal irritation. Hysterectomy and bilateral salpingo-oöphorectomy is recommended rather than simple removal of the affected tube. The question of post-operative irradiation is undecided and prognosis doubtful.

F. J. Browne

549. **Confluent Intertubal Serous Cyst.** (Sierocele intertubarico confluente.)

By U. CASABONA. *Ginecologia, Torino,* **13**, 1–16, Jan. 1947. 10 figs., 18 refs.

See also No. 410.

Operations

550. **Thrombophlebitis and Phlebothrombosis in Gynecologic Patients; the Prophylaxis, Recognition, and Treatment.**

By J. V. MEIGS and F. M. INGERSOLL. *Amer. J. Obstet. Gynec.*, **52**, 938–945, 959–963, Dec. 1946. 9 refs.

In the surgical wards of the Massachusetts General Hospital, in spite of conservative preventative measures such as the control of posture and the use of exercises, fatal embolism occurred in 1 out of 800 patients undergoing major surgical operations. Because of this danger a means has been sought to prevent embolism after operation, and with that end in view 1,057 ligations of the superficial femoral vein have been done in the hospital since 1937. It had been shown by Castleman that nearly all fatal emboli come from the veins of the legs. At present the consensus in the hospital is that failure to ligate at once the veins of a patient who has had a non-fatal pulmonary embolus, or a patient who has definite signs of either thrombophlebitis or phlebothrombosis, constitutes serious neglect. In the gynaecological wards in the 5 years 1941–5 there were 3,503 operations and 75 vein ligations. Death from emboli occurred in 5 cases, in only 1 of which the vein had been interrupted.

The general plan in the hospital is to try to prevent pulmonary embolism by ligation of the appropriate veins in patients who have a suggestion of thrombophlebitis or phlebothrombosis, and to interrupt definitely the femoral veins of those patients who have had a sublethal pulmonary embolus or infarct. Early diagnosis is essential. If any tenderness is found or if the patient complains of pain in her legs, the groin, inside of thigh, popliteal space, calf, and veins of foot are palpated for tenderness or swelling. The most important sign is tenderness of the calf, which was present in 53 per cent of the 75 patients in whom the veins were ligated. A positive Homans's sign (pain in the calf on dorsiflexion of the foot) is diagnostic but was only present in 28 per cent of the 75 cases. Swelling of the leg is important, while a rise in pulse rate, temperature, and respiration rate in addition to other physical findings suggests the presence of a small pulmonary infarct.

Various methods have been tried to prevent venous thrombosis. Early movements, elevation of the foot of the bed, and anticoagulants are being tried out with careful controls. The surgical treatment of thrombophlebitis and phlebothrombosis consists in the interruption of the vein above the clot. Both legs must be operated on. A 4-in. (10 cm.) incision is made from the groin downwards along the course of the femoral artery. The subcutaneous tissue, superficial fascia, and fascia lata are divided. The femoral pulsation is felt for, and deep to the sartorius muscle and lying on the adductor longus the femoral artery and vein are found. The sheath overlying the vessels is approached from the medial side and the sheath surrounding the vein opened. Inside the sheath the dissection is carried upwards and the superficial femoral vein isolated over a 4-cm. length. Ligatures are placed under it and not tied but held on tension, and the vein opened. Tension is then released when there should be a free flow of blood. If there is not, a suction tube is inserted into the common femoral and suction applied. After the vein is sucked out and a free flow of blood occurs the common femoral and iliac veins are considered to be cleared. The vein is then tied just below the profunda. If the superficial femoral and the pro-

funda are both involved in the thrombosis, it is essential to tie the common femoral vein. "Emboli have followed interruption of the veins, but few have been fatal. . . If emboli do occur they are not fatal, and the use of dicoumarol has prevented further emboli."

F. J. Browne

551. **Phlebothrombosis and Thrombophlebitis in Gynecology and Obstetrics.**

By C. G. COLLINS and E. W. NELSON. *Amer. J. Obstet. Gynec,* **52**, 946-963, Dec. 1946. 82 refs.

Intravenous clotting may be associated with two conditions—phlebothrombosis and thrombophlebitis. In the former there is no inflammation, and the clot is loosely attached to the vein wall. Because of this it is liable to break away and give rise to a pulmonary infarct. In thrombophlebitis, on the other hand, the clot is firmly adherent, and, unless suppuration is present, rarely results in pulmonary infarction or embolism.

In phlebothrombosis there is usually little or no swelling, pain, or fever and sometimes pulmonary infarction is the first symptom. Any persistent or undue elevation of pulse rate or temperature should arouse suspicion, and repeated examinations for clinical signs of phlebothrombosis should be made. Examinations of the legs should be a part of the routine care of patients confined to bed. A complaint of pain in the chest or in the lower limbs should not be lightly dismissed. In some cases oedema of the leg is found in phlebothrombosis, especially if the common femoral vein is involved. This is often the case with tumours of the pelvis, in which oedema is apt to be ascribed to pressure by the tumour. Any case of unilateral oedema, and particularly if associated with pregnancy or pelvic tumours, should be considered due to phlebothrombosis of the femoral or pelvic veins until proved otherwise. As to treatment, the "horse and buggy" therapy by elevation of the leg and wrapping it in cotton "batting" is still too often used; it does not prevent pulmonary infarction. Modern treatment consists of either venous ligation or the use of anticoagulants. The authors have had no experience of the latter method.

The diagnosis of thrombophlebitis (phlegmasia alba dolens) is not difficult. Usually fever is present with pain and oedema and tenderness along the course of the vein; if deep veins are involved, especially the femoro-iliac, there is pallor and cyanosis. These symptoms are due not to venous blockage but to reflex vasospasm, resulting in decreased pulsation in the arteries of the limb, increased capillary permeability, and exudation of fluid into the extravascular tissues. Such cases are treated by blocking the sympathetic nerve supply to the involved extremity by procaine hydrochloride. The relief of pain is dramatic, while fever and oedema rapidly subside.

Suppurative thrombophlebitis of the pelvic veins is most often found in cases of puerperal sepsis, though it may follow application of radium, suppurative process in the adnexa, or gynaecological operations. Detachment of the clot sometimes occurs with pulmonary infarction, the suppurative process of the clot causing liquefaction. In one such case after vaginal hysterectomy vena cava ligation was performed; the patient recovered and there were no untoward after-effects. The authors favour ligation of the ovarian vein and inferior vena cava in all cases of suppurative pelvic thrombophlebitis which fail to respond to conservative therapy, including sulphonamides and penicillin. A definite diagnosis of suppurative pelvic thrombophlebitis is fairly difficult to make. "Spiking" fever and chills are often, but not always, present. Occasionally there is a plateau-like temperature curve, and chills may be absent. A fairly constant finding is an elevated pulse rate in a patient who looks less ill than the history and findings would indicate. On vaginal examination little or no exudate is found in the parametrium; sometimes thrombosed veins may be felt there or in the vaginal wall. All lung infarcts do not produce the typical pleural pain and bloody sputum, and they may only be detected by radiographs, though Krause states that "the roentgen diagnosis of pulmonary infarct is probably subject to a greater percentage of error than that of any other lesion of the lung". Positive blood cultures are of value, especially in determining whether the organism is penicillin-sensitive, but negative ones do not rule out the presence of suppurative pelvic thrombophlebitis. In the authors' series palpable thrombosed vaginal or pelvic veins were found on vaginal examination in only 36 per cent of the cases. No deaths occurred in the ligations following gynaecological operations, but in ligations for puerperal suppurative thrombophlebitis there were 2 deaths (13.5 per cent). In

both cases the ligation was too long delayed in the the hope that penicillin and sulphonamides might effect a cure. No ill-results, such as oedema, seemed to follow the ligation of the inferior vena cava. This freedom from after-effects is, in the authors' opinion, due to the fact that they routinely carried out paralumbar sympathetic block, or, in their later cases, sectioned the right and left sympathetic chains at the time of ligation.

In the discussion that followed this paper and that of Meigs and Ingersoll (see Abstract 549) Curtis condemned venous ligation as an unnecessary procedure. Heparin and dicoumarol therapy he believed to be simpler, safer, and more satisfactory. Masson considered it difficult to decide what veins should be ligated; he said that the " promiscuous ligation of major veins as a prophylactic measure is not warranted, especially in view of the possible sequelae that may be a definite handicap to the patient in future years ".

F. J. Browne

532. **Investigations on the Uterine Mucosa. I. Biopsy Material, its Treatment and Evaluation.** [In English.]

By B. FALCONER. *Acta obstet. gynec. scand.*, **26**, 453–474, 1946. 8 figs., 28 refs.

Investigations on the Uterine Mucosa. II. The Occurrence and Significance of Ectatic and Cystic Glands in the Uterine Mucosa. [In English.]

By B. FALCONER. *Acta obstet. gynec. scand.*, **26**, 475–495, 1946. 2 figs., 12 refs.

Investigations on the Uterine Mucosa. III. On the Early Diagnosis of Metropathia Haemorrhagica. [In English.]

By B. FALCONER. *Acta obstet. gynec. scand.*, **26**, 525–545, 1946. 10 figs., 7 refs.

In this series of articles the author reviews the methods of obtaining biopsy material from the uterus and the methods of examining it. He has used the facilities of the Department of Women's Diseases at Stockholm and the Department of Gynaecology at the Radiumhemmet to obtain specimens.

The characteristic changes in curetted material are fresh haemorrhages, signs of invaginations of the glands, and cadaveric processes of varying degree. The author believes that invagination, being found in the basalis, is not merely an artefact but is partly conditioned by the firm stroma of the basalis or is a sign of glandular hyperplasia. Modern methods of obtaining strip curettings by suction or cannula are open to many criticisms from the pathologist, however useful they may be to the clinician. As the author puts it: " It would be, of course, unreasonable to judge the quality of the wallpaper of a room by a sample taken offhand." Suction curettage, too, leads to fresh blood extravasations. In a discussion of the various staining techniques the difficulties of assessing the secretory contents of the glands are emphasized.

Ectatic and cystic glands were found in 20 cases during the reproductive period of life. They occur in the presence of hypoplasia, hyperplasia glandularis cystica, endometritis, atrophy, and in the angle between a myoma and the underlying uterine wall. Ten of the patients had definite pathological conditions—myoma 2, endocrine dysfunction 4, hyperplasia 4. The other 10 patients had cysts not associated with such easily explained causes, but 5 were women who had had recurrent miscarriages and 5 were sterile women. The author considers such cysts to be a symptom of ovarian insufficiency.

Finally, the author discusses the early pathological changes found in the cystic hyperplasia of metropathia haemorrhagica. All patients in whom the diagnosis had been made have been followed up and further biopsies obtained. Fluhman's work is accepted as a basis of the histological appearances. The author believes that the characteristics of early hyperplasia are: (1) epithelial: increase in the number of cells, packing together of cells, signs of invagination, dilated and cystic glands, epithelial cells with elongated nuclei; and (2) mesenchymal: hyperplasia confined to well-defined areas, cells of " the prematurely ripe type rich in fibrils, lymphatics, and dilated blood vessels ". Six cases of early glandular hyperplasia are fully described clinically and histologically.

[This series of papers forms most interesting reading and is welcome as the cases are fully followed up. It provides an up-to-date account of the aspects of curetting with which it deals.]

Kenneth Bowes

553. **Injuries Caused by Hysterosalpingography.** [In English.]

By P. HOLM-NIELSEN. *Acta obstet. gynec. scand.*, **26**, 565–597, 1946. 39 refs.

The author has made an exhaustive study of the complications of lipiodol insufflation of the

Fallopian tubes. The literature is first reviewed in detail, and then an analysis of replies to a questionary (covering about 12,000 cases) sent to all Danish hospitals is described. Finally, 1,100 operations during the last 4½ years at the Aarhus Municipal Hospital are investigated. The most frequent complications are inflammatory (0.25 per cent), and these usually consist of a recurrence of previous infection. The iodized oil is not considered to be incriminated. When at a later date laparotomy has followed lipiodol insufflation, minor adhesions have been found in the pelvis with small granulomatous areas on the peritoneum. These changes are not important. "Iodism" has not been met with in any case. There were only 5 cases of oil embolism and in none did the patient suffer discomfort. No proof was found that tubal pregnancy was likely to follow the operation.

The author concludes that although hysterosalpingography is a minor operation its performance entails definite risks, but that these are far outweighed by its usefulness both in diagnosis and in treatment.

Braithwaite Rickford

554. **Oil Embolism Following Hysterosalpingography.**

By F. M. INGERSOLL and L. L. ROBBINS. *Amer. J. Obstet. Gynec.*, **53**, 307–311, Feb. 1947. 3 figs., 9 refs.

555. **Uterosalpingography. Report of a Fatality.**

By A. M. FARIS and A. MCMURREY. *Tex. St. J. Med.*, **42**, 592–597, Feb. 1947. 9 figs., 13 refs.

556. **Surgery of Perforation of the Uterus with Severe Intestinal Lesions.** (Sulla chirurgia delle perforazioni dell'utero con gravi lesioni intestinali.)

By A. BILLI. *Clin. ostet. ginec.*, **49**, 30–35, Jan.-Feb., 1947. 3 figs.

557. **Plastic Operations in Hysterectomy.**

By O. S. COFER. *Sth. med. J.*, **40**, 31–36, Jan. 1947. 8 figs., 5 refs.

One hundred cases of vaginal hysterectomy, in all of which an anterior colporrhaphy, a perineorrhaphy, and in some instances additional plastic operations for control of urinary incontinence, rectocele, or cystocele, were performed more than 5 years previously, are compared with 100 cases in which similar operations have been performed in the last 5 years. The cases are selected and not consecutive. Though the different time factor in the two series will invalidate some comparisons, shortening of the vagina, which was particularly common in the first group, is unaffected by time. The comparative table below indicates the results obtained.

	Over 5 years	Under 5 years
Shortened vagina	25	3
Stress incontinence before operation	36	42
Relieved by Kelly operation ...	24	40
Stress incontinence after operation (not present before)	8	0
Vaginal-vault prolapse recurrence, with cystocele and rectocele ...	16	2
Total cases	100	100

The author's operative technique is explained in detail. This largely follows the modifications of Mayo or of Goffe and Ward, and particular attention is paid to the shaping of the epithelial flaps of the vagina to be removed in order to lengthen both the anterior and posterior vaginal walls. The author believes in fixing the bladder neck vaginally to relieve stress incontinence by using the method of Kennedy and Counseller. [This involves mobilizing the urethra, and must subsequently give rise to increased fibrosis and fixation.]

D. M. Stern

558. **Bacteriology of Vagina in Total Hysterectomy.**

By C. J. DUNCAN. *Amer. J. Obstet. Gynec.*, **53**, 324–325, Feb. 1947.

559. **Frequency of Carcinoma in a Residual Cervical Stump and Mortality from Total Hysterectomy as Compared with that from Subtotal Hysterectomy.** (Frequenza del carcinoma sul moncone residuo e mortalità dell'isterectomia totale nei confronti dell subtotale.)

By C. CANTONE. *Ginecologia, Torino*, **12**, 285–295, Sept. 1946.

560. **An Operative Procedure for the Repair of the Urethrodiverticulovaginal Fistula. Report of Two Cases.**

By W. W. SCOTT and W. L. EKAS. *Surgery*, **20**, 645–655, Nov. 1946. 10 figs., 3 refs.

The authors describe in detail the clinical findings and operative technique in 2 cases of this very rare condition, which they call urethro-diverticulovaginal fistula. In a review of the literature they

could find only 2 other cases described. The condition is acquired. The patients complain of frequency and urgency of micturition, dysuria, and urinary obstruction in varying degree. As the fistula leads also to urinary incontinence, it is important that it should be remembered when vesico-vaginal or uretero-vaginal fistula has been excluded. The article explains by means of diagrams the operative technique of repair.

[The urologist and the gynaecologist will be interested to read of this condition, particularly at this time, when more interest is being evinced in the anatomy, physiology, and pathology of the female urethra.]

G. Gordon Lennon

561. **The Artificial Autotransplantation of Endometrium in Supra-vaginal Amputation of Uterine Myoma.**

By R. BUDIMLICH. *Srpski Arkhiv.*, **45**, 21–25, Jan. 1947.

562. **A Modification of the Plastic Operation on the Pyramidalis Fascia in Urinary Incontinence. Operation by the Abdominal Route only. Report on Three Cases.** [In English.]

By A. SJÖVALL. *Acta obstet. gynec. scand.*, **26**, 546–554, 1946. 5 refs.

Three cases of stress incontinence treated by Sunde's modification of the Goebel-Stoeckel operation are described. A single fascial strip 4 cm. wide is taken in the midline from the umbilicus to the pyramidalis (if present). This length of fascia is drawn beneath the bladder neck and sutured to its origin near the symphysis pubis. Damage to the urethra is avoided by injecting 4 ml. of local anaesthetic solution between the anterior vaginal wall and the urethra. Also a finger is kept in the vagina to palpate the passage of the forceps as it is passed from above beneath the urethra. All the cases made good progress, and the symptoms remained cured during the period of a short follow-up. Stress is laid upon the avoidance of infection of the prevesical cellular tissue, and therefore of sloughing the fascia, by using the single abdominal incision and not opening the infected anterior vaginal wall.

[Fascial sling operations such as the Millin sling and Aldridge operation are very popular at the moment. The author states that the indications for the operation are: (1) failure of a previous anterior colporrhaphy and suburethral repair; and (2) virginity or multiparity of the patient. A third type of patient for whom the operation is indicated might be added—the chronic bronchitic who is rarely if ever free from cough. The risks of infection from a vaginal incision have been overrated and would seem to be less than those of urethral damage.]

Braithwaite Rickford

563. **Suprapubic Transvesical Repair of Vesico-vaginal Fistula.**

By R. F. SHARP and M. M. GREEN. *Urol. cutan. Rev.*, **50**, 632–636, Oct. 1946. 3 figs., 10 refs.

There are three methods of approach in the treatment of vesicovaginal fistula—namely, vaginal, transperitoneal, and transvesical. There are certain indications for the suprapubic transvesical approach. The bladder must be carefully examined by cystoscopy and the size, location, and number of openings must be accurately determined. The indications are listed as follows: (1) A fistula high in the vaginal vault, especially after a total hysterectomy where no cervix remains and the operator therefore cannot pull the operative field downwards and facilitate the vaginal exposure. (2) A contracted and narrow vaginal vault. (3) In the presence of a uretero-vaginal fistula. (4) A fistula close to a ureteric orifice which might be included in a blind vaginal approach. (5) Where stones, polypi, or aberrant bands of tissue in the bladder require surgical treatment. (6) Where the opening to the bladder communicates with the cervical canal. (7) Where a vaginal operation has failed.

As the operation is one of election the patient's general condition must, if necessary, be built up before operation. The authors prefer spinal analgesia. A toilet is done of the vagina and a large gauze roll is inserted, one end being left out so that it may easily be withdrawn by a non-sterile operating-room assistant. The purpose of this pack is to elevate the bladder and make the operation field more accessible. A sub-umbilical midline incision is made, and the bladder exposed and opened widely. If the opening of the fistula is near a ureteric orifice a catheter is passed along the uretero. The tract is completely excised by means of a circular incision approximately 2 mm. from its margin. A line of cleavage is then developed

between the bladder and the vaginal walls: this is probably the most difficult part of the operation. It may be necessary to make a sagittal incision through the whole detrusor portion of the bladder in order to obtain sufficient mobility of the floor to close the opening without tension. The vagina and bladder are closed in layers, No. oo chromic interrupted sutures being used. The anterior incision in the bladder wall is closed around a large de Pezzer catheter.

A. W. Badenoch

See also Nos. 443, 487, 488, 499, 501, 502, 529, 530.

Miscellaneous.

564. **Hernia of the Internal Female Genitalia.** (Sulle ernie dei genitali interni femminili.)
By P. ALFIERI. *Clin. ostet. ginec.*, **49**, 22–29, Jan.–Feb. 1947. 2 figs., 34 refs.

565. **Peritoneal Uterine Fissure due to Spontaneous Rupture of Subserous Vessels in General Fragility of the Veins.** (Fissura uteri peritonealis durch Spontanruptur subseröser Gefässe bei allgemeiner Venenschwäche.)
By H. K. v. RECHENBERG. *Schweiz. med. Wchsr.*, **77**, 357–359, Mar. 22, 1947. 9 refs.

566. **Vesicovaginal Fistulae.**
By I. YOVANOVICH and D. YEREMICH.
Srpski Arkhiv., **45**, 25–31, Jan., 1947. 7 refs.

567. **Spontaneous Closure of Post-irradiation Vesicovaginal Fistula. Case Report.**
By G. C. MILNOR. *Proc. Clin., Honolulu*, **12**, 207–208, Dec. 1946.

568. **540 Cases of Genital Prolapse Observed at the Gynaecological Clinic of the School of Medicine. University of Bahia (1911-1946).** (Revisao de 540 casos de prolapso genital observados na clínica ginecológica da faculdade de medicina de Bahia, desde a sua criação até hoje [1911–1946].)
By A. PELTIER DE QUEIROZ. *An. brasil, Ginecol.*, **22**, 435–452, Dec. 1946. 7 figs., 5 refs.

569. **Chronic Uterine Inversion.** (Inversión uterina crónica.)
By H. CABRERA. *Bol. Soc. chil. Obstet. Ginec.*, **11**, 183–185, Oct. 1946. 5 refs.

570. **Massive Intraperitoneal Hemorrhage Caused by Rupture of Hemorrhagic Corpus Luteum.**
By E. B. PEDLOW. *Ohio St. med. J.*, **43**, 168–169, Feb. 1947. 1 fig., 1 ref.

571. **Leucoplakia Vulvae. Its Etiology and Results of Treatment with Vitamin A. Preliminary Report.**
By M. N. HYAMS and O. H. BLOOM. *Amer. J. Obstet Gynec.*, **53**, 214-220, Feb. 1947. 6 figs., 4 refs.

The authors investigated a group of 18 patients at New York Post-Graduate Hospital in all of whom the diagnosis of leucoplakia vulvae had been verified by histological examination. The only significant finding was that 60 per cent of the cases had little or no hydrochloric acid in the gastric contents. As anacidity and subacidity of the gastric contents are associated with low plasma content of vitamin A, the authors treated the patients with 250,000 to 500,000 units daily by mouth, supplemented by twice-weekly injections of 50,000 units. In addition each patient was given 15 minims of dilute hydrochloric acid in water three times daily. Fourteen patients improved objectively and subjectively. In the other cases, which were unimproved, there was in addition some constitutional disease—diabetes (2), syphilis (1), and cardio-renal vascular lesion (1).

Gladys Dodds